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OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: 23-FEB-2011

SUBJECT: Difenoconazole. Application for Amended Section 3 Registration to Add Uses on Carrots, Chickpeas, Soybeans, Stone Fruits (Group 12), Strawberries, and Turnip Greens. Summary of Analytical Chemistry and Residue Data.

PC Code: 128847
Decision No.: 426124
Petition No.: PP#9F7676
Risk Assessment Type: NA
TXR No.: NA
MRID No.: See MRID Summary Table
Ver.Apr.08

DP Barcode: 378829
Registration Nos.: 100-1262, 100-1312, 100-1313, and 100-1317
Regulatory Action: Amended Section 3 Registration
Case No.: 7014
CAS No.: 119446-68-3
40 CFR: 180.475

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MRID Summary Table		
MRID No.	**Study Type**	**Comments**
47929801	860.1500 Soybean	New DER 47929801.de1.doc
	860.1520 Soybean processing	New DER 47929801.de2.doc
47929802	860.1500 Strawberry	New DER 47929802.der.doc
47929803	860.1500 Stone fruit	New DER 47929803.de1.doc
	860.1520 Plum processing	New DER 47929803.de2.doc
47929804	860.1500 Carrot	New DER 47929804.der.doc
47929805	860.1500 Chickpea	New DER 47929805.der.doc

This document has been prepared by the Health Effects Division (HED) and reflects current Office of Pesticide Programs (OPP) policies.

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Executive Summary

Difenoconazole is a broad spectrum fungicide belonging to the triazole group of fungicides (Group 3). It is currently registered in the U.S. for use as a seed treatment on cereal grains, canola, and cotton and for foliar applications on numerous crops. The mode of action of difenoconazole is as a demethylation inhibitor of sterol biosynthesis which disrupts membrane synthesis by blocking demethylation.

Under PP#9F7676, Syngenta Crop Protection, Inc. is proposing the establishment of tolerances for residues of difenoconazole [1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole] in/on the following raw agricultural commodities:

Carrot ....0.45 ppm
Chickpeas..0.05 ppm
Soybean, seed..0.20 ppm
Soybean, aspirated grain fraction....................................95 ppm
Fruits, stone, group 12 ....2.5 ppm
Strawberry ....2.5 ppm

Also, in compliance with a previous HED recommendation (PP# 8F7482; DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian), Syngenta Crop Protection, Inc. is also proposing the establishment of a tolerance for residues of difenoconazole [1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole] in/on the following raw agricultural commodity:

Turnip greens ....35 ppm[1]

[1] According to the "Reviewer's Guide and Summary of HED ChemSAC Approvals for Amending Crop Group/Subgroups [40 CFR 180.41] and Commodity Definitions [40 CFR 180.1(h)]" June 14, 2006, mustard greens data may be used to support a tolerance on turnip greens since it has been recommended that turnip greens be moved into the crop subgroup 5B (Rep Crop = mustard greens).

Syngenta Crop Protection, Inc. is also requesting that the established tolerance for residues of difenoconazole [1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole] in milk be increased from 0.01ppm to 0.08 ppm due to the introduction of new livestock feedstuffs with this petition:

Milk..0.08 ppm

In conjunction with PP#9F7676, Syngenta Crop Protection, Inc. is proposing an amended Section 3 registration for a 2.08 lb/gal emulsifiable concentrate (EC) formulation (Inspire™ Fungicide; 100-1262) to add uses on carrots, chickpeas, soybeans, stone fruits, and strawberries. In addition, Syngenta Crop Protection, Inc. is proposing to add some or all of these proposed uses to the following multiple active ingredient (MAI) products: a 2.08 lb/gal MAI EC formulation with propiconazole (Inspire™ XT Fungicide; EPA Reg. No. 100-1312); a 1.05 lb/gal MAI suspension concentrate (SC) formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313); and a 0.73 lb/gal MAI emulsion oil in water (EW) formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317). The EC product formulations (EPA Reg. Nos. 100-1262 and 100-1312) are proposed for multiple foliar applications at 0.09-0.114 lb ai/A/application for maximum seasonal rates of 0.46 lb ai/A on carrots, chickpeas (EPA Reg. No. 100-1262 but not EPA Reg. No. 100-1312), soybeans, stone fruits, and strawberries. The proposed minimum preharvest intervals (PHIs) are 7 days for carrots (14 days for EPA Reg. No. 100-1312), 14 days for chickpeas and soybeans, and 0 days for stone fruits and strawberries. The SC formulation product (EPA Reg. No. 100-1313) and the EW formulation product (EPA Reg. No. 100-1317) are proposed for the same crops, except that the EW formulation is not proposed for use on soybeans, with essentially the same use patterns and the same minimum PHIs. There is a proposed restriction against the feeding of soybean hay, forage and silage which is considered to be under grower control.

None of the proposed labels lists turnip greens as a separate use site; however, the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 1.05 lb/gal MAI SC formulation with azoxytrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313), and the 0.73 lb/gal MAI EW formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317) include use directions for Brassica leafy vegetables. None of the proposed labels lists turnip greens as a commodity under Brassica leafy vegetables.

Three of the difenoconazole products addressed herein contain a second active ingredient (propiconazole, azoxystrobin, or cyprodinil). The subject review addresses the proposed uses for difenoconazole only.

Tolerances for difenoconazole are currently established under 40 CFR §180.475. Tolerances for plant commodities are established under §180.475(a)(1) and are expressed in terms of difenoconazole *per se*. Tolerances are established for numerous raw agricultural and processed commodities and range from 0.01-35 ppm; import tolerances are established for banana, papaya, and rye grain, and range from 0.10-0.30 ppm. Tolerances for livestock commodities are established under §180.475(a)(2) and are expressed in terms of difenoconazole and its metabolite, CGA-205375 [1-[2-chloro-4-(4-chloro-phenoxy)phenyl]-2-[1,2,4]triazol-1-yl-ethanol]; tolerances for tissue, milk, and egg range from 0.01-0.20 ppm.

Because difenoconazole is a triazole compound, HED requires that samples from any metabolism, field trial, and/or processing study be analyzed for the triazole metabolites triazolylalanine (TA), triazolyl acetic acid (TAA), and 1,2,4-triazole (1,2,4-T). HED issued guidance on the residue chemistry data requirements for the triazole-based metabolites under DP# 327788 (4/25/06, M. Doherty). The studies submitted with this petition reflect analysis for the three triazole metabolites.

The nature of the residue in plants is understood based on acceptable plant metabolism studies reflecting foliar applications in canola, grape, potato, tomato, and wheat, and seed treatment in wheat. HED concludes that the residue of concern for both tolerance enforcement and risk assessment for crops included in this petition is difenoconazole *per se*. The nature of the residue in livestock is understood based on acceptable goat and hen metabolism studies. The residues of concern for both tolerance setting and risk assessment for livestock commodities are difenoconazole *per se* and its metabolite CGA-205375.

An adequate tolerance enforcement method, Method AG-575B, is available for crop commodities. The method determines residues of difenoconazole *per se* in/on crop commodities by gas chromatography with nitrogen-phosphorus detection (GC/NPD). The method limits of quantitation (LOQs) are 0.01-0.05 ppm. A confirmatory GC method with mass-selective detection (MSD) is also available for crop commodities.

An adequate tolerance enforcement method, Method REM 147.07b, is available for livestock commodities. The method determines residues of difenoconazole and CGA-205375 in livestock commodities by liquid chromatography with tandem mass spectrometry detection (LC/MS/MS). The method LOQs are 0.01 ppm (for each analyte) for livestock tissues and 0.005 ppm (for each analyte) for milk; these LOQs are lower than the LOQs of the former tolerance enforcement method which was in place when livestock tolerances were last amended (PP# 6F7115; D340379, 8/9/07, W. Wassell and M. Sahafeyan). Adequate confirmatory methods, Method AG-544A and Method REM 147.06, are available for the determination of residues of difenoconazole and CGA-205375, respectively, in livestock commodities.

Samples from the submitted crop field trials and processing studies were analyzed for residues of difenoconazole using a high performance liquid chromatography method with tandem mass spectrometry detection (LC/MS/MS), Method REM 147.08, and for residue of the triazole metabolites TA, TAA, and 1,2,4-T using Morse Laboratories LC/MS/MS method Meth-160, Revision #2. The methods were adequate for data collection based on acceptable concurrent method recoveries. The LOQ was 0.01 ppm for each analyte in each commodity.

There are several cattle feedstuffs associated with the proposed uses: carrot culls (considered an alternative feedstuff), soybean seed, soybean meal, soybean hulls and soybean aspirated grain fractions (AGF). There are two swine and poultry feedstuffs associated with the proposed uses: soybean seed and soybean meal. Adequate feeding study data have been submitted previously for difenoconazole in cattle and poultry commodities. Based on the calculated dietary burdens and the feeding study data, HED concludes that the currently established livestock tolerances for milk, meat, fat, and meat byproducts (except liver) are adequate to support the proposed uses; however, due primarily to the significant change in the beef diet from the proposed use on soybeans and the residues of difenoconazole found in/on soybean AGF, the tolerance levels for residues of concern in liver of cattle, goat, hog, horse, and sheep should be increased from 0.20 ppm to 0.40 ppm. Also, although there was little change in the poultry diet from the new uses, due to the LOQs of the current livestock enforcement method, the tolerance level for residues of concern in egg, should be decreased from 0.10 ppm to 0.02 ppm. Note: The new tolerance level in egg is set at the combined LOQ (0.02 ppm; 0.01 ppm for each analyte) of the current livestock tolerance enforcement method (Method REM 147.07b) which is lower than that of the former enforcement method.

Supporting storage stability data were not provided in the subject submissions; however, available storage stability data for residues of difenoconazole *per se* in/on various raw agricultural crop, processed, and livestock commodities are deemed adequate to support the storage conditions and durations of samples from the crop field trial and processing studies reviewed herein and the livestock feeding studies re-evaluated herein. No supporting storage stability data were provided for the triazole metabolites in the current submission; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (D363016) and these data are expected to satisfy storage stability data requirements for the subject petition. Also, because previously submitted cattle and poultry feeding studies were re-evaluated for the subject petition, supporting storage stability data for residues of 1,2,4-triazole (1,2,4-T) are required to support the storage conditions (frozen) and intervals (up to 10 months) of livestock commodity samples collected for the cattle and poultry feeding studies. However, storage stability data for these compounds have been requested as part of the Human Health Aggregate Risk Assessment for the triazole metabolites (M.Doherty, *et al.*, 2/7/06) and these data, when submitted, are expected to satisfy storage stability data requirements for the subject petition.

Provided the petitioner submits a revised Section B/proposed labels specifying a minimum retreatment interval (RTI) of 14-days for chickpeas and a maximum seasonal use rate of 0.22 lb ai/A for soybeans, adequate field trial data have been submitted to support the proposed uses of the EC formulations of difenoconazole on carrots, chickpeas, soybeans, stone fruits, and strawberries. The submitted data will support the proposed tolerances for stone fruits, group 12 (2.5 ppm) and strawberries (2.5 ppm). The proposed tolerances for carrots (0.45 ppm) and chickpeas (0.05 ppm) are too low; tolerances of 0.50 ppm and 0.08 ppm, respectively, are appropriate. The proposed tolerance for soybean seed (0.20 ppm) is too high; a tolerance of 0.15 ppm is appropriate.

The petitioner is also requesting the use of a 1.05 lb/gal suspension concentrate (SC) formulation of difenoconazole and a 0.73 lb/gal emulsion oil in water (EW) formulation of difenoconazole on carrots, chickpeas, soybean (excluding the EW formulation), stone fruits, and strawberries with essentially the same use pattern and minimum PHI. However, no carrot, chickpea, soybean, stone fruit, and strawberry field trial data have been generated with these formulations. The petitioner has previously submitted side-by-side field trial data for leaf lettuce, mustard greens, and tomatoes comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 2.08 lb/gal SC formulation or with that of a 0.73 lb/gal EW formulation (DP# 354013, 3/20/09, B. Cropp-Kohlligian).

With regards to the proposed uses of the SC formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries, having considered the available residue database for difenoconazole which indicates that the recommended tolerances for residues of difenoconazole in/on carrots, chickpeas, stone fruits, and strawberries are based on large datasets, with the exception of chickpeas, and calculated using the tolerance spreadsheet at levels well above the maximum residue level found in the supporting magnitude of the residue data, HED concludes that the recommended tolerances for residues of difenoconazole in/on carrots (0.50 ppm), chickpeas (0.08 ppm), stone fruits (2.5 ppm), and strawberries (2.5 ppm) are likely to cover the proposed uses of the 1.05 lb/gal SC formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries. These conclusions are supported by the previously submitted leaf lettuce, mustard greens, and tomatoes side-by-side field trial data comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 2.08 lb/gal SC formulation. The submitted field trial data representing an EC formulation of difenoconazole are, therefore, deemed adequate to support the proposed uses of the SC formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries provided the petitioner submits a revised Section B/proposed label specifying a minimum RTI of 14-days for chickpeas.

With regards to the proposed use of the SC formulation of difenoconazole on soybeans, the available leaf lettuce, mustard greens, and tomatoes side-by-side field trial data comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 2.08 lb/gal SC formulation and reflecting a 0-day PHI are <u>not</u> adequate to support the proposed use of the 1.05 lb/gal SC formulation on soybean seeds, which includes a significantly longer PHI (14-days). [Note: There is a proposed restriction against the feeding of soybean hay, forage and silage which is considered to be under grower control.] Furthermore, having considered the available residue database for difenoconazole which indicates that the recommended tolerance for residues of difenoconazole in/on soybean seeds (0.15 ppm) is based on a large dataset and calculated using the tolerance spreadsheet at a level equal to the maximum residue level (0.152 ppm), but well above the highest average field trial (HAFT) level (0.0869 ppm), found in the supporting magnitude of the residue data, additional soybean field trials conducted with the SC formulation at the maximum proposed use rate are required. These additional data are considered confirmatory since, in the meantime, HED concludes that the recommended tolerance for residues of difenoconazole in/on soybean seed (0.15 ppm) is likely to cover the proposed use of the SC formulation of difenoconazole on soybeans provided the petitioner submits a revised Section B/proposed label specifying a maximum seasonal use rate of 0.22 lb ai/A for soybeans.

With regards to the proposed uses of the EW formulation of difenoconazole, having considered the available residue database for difenoconazole which indicates that the recommended tolerances for residues of difenoconazole in/on carrots, chickpeas, stone fruits, and strawberries are based on large datasets, with the exception of chickpeas, and calculated using the tolerance spreadsheet at levels well above the maximum residue level found in the supporting magnitude of the residue data, HED concludes that the recommended tolerances for residues of difenoconazole in/on carrots (0.50 ppm), chickpeas (0.08 ppm), stone fruits (2.5 ppm), and strawberries (2.5 ppm) are likely to cover the proposed uses of the 0.73 lb/gal EW formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries. However, given the potential for the 0.73 lb/gal EW formulation to produce higher residues of difenoconazole than the EC formulation, as suggested by the previously submitted side-by-side field trial data, and in the absence of sufficient data to fully dispel concerns for that potential in/on carrots, chickpeas, stone fruits, and strawberries, additional data for the 0.73 lb/gal EW formulation of difenoconazole should be submitted as confirmatory evidence. As recommended by ChemSAC (meeting 01/27/2010), additional side-by-side field trials on grapes comparing difenoconazole residues resulting from applications of the EC and EW formulations should provide a more complete and robust dataset to serve as a surrogate for potential residual differences in/on fruits and vegetables at issue. In the meantime, the submitted field trial data representing an EC formulation of difenoconazole are also deemed adequate to support the proposed uses of the EW formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries provided the petitioner submits a revised Section B/proposed label specifying a minimum RTI of 14-days for chickpeas.

No turnip green data were provided in the subject submission. In compliance with a previous HED recommendation (PP# 8F7482; DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian), the petitioner is proposing the establishment of a tolerance for residues of difenoconazole in/on turnip greens at 35 ppm. Available mustard greens data for difenoconazole will be translated to support a tolerance for residues of difenoconazole in/on turnip greens at 35 ppm.

Adequate processing data for plum and soybean have been submitted to support the proposed uses on stone fruits and soybeans. The plum processing data indicate that residues of difenoconazole *per se* do concentrate in prunes. However, based on the highest average field trial (HAFT) level for residues in/on plums (0.543 ppm) and the average processing factor (2.6x), residues in/on prunes are expected to be lower than the recommended 2.5 ppm tolerance for stone fruits; hence, a separate tolerance is not needed for residues of difenoconazole in prunes. The soybean processing data indicate that residues of difenoconazole *per se* do concentrate in hulls and aspirated grain fractions (AGF), but do <u>not</u> concentrate in meal and refined oil. Although none was proposed by the petitioner, based on the HAFT level for residues in/on soybean seed (0.0869 ppm) and the average processing factor for hulls (2.0x), a separate tolerance is needed for residues of difenoconazole in/on soybean hulls at 0.20 ppm. Consistent with the tolerance level proposed by the petitioner for AGF and based on the recommended tolerance in/on soybean seed (0.15 ppm) and the average processing factor for AGF (622x), a tolerance is needed for residues of difenoconazole in/on AGF at 95 ppm.

The nature of the residue in rotational crops is not adequately understood because previously conducted studies did not reflect sufficiently high application rates, and/or insufficient characterization/identification of residues was achieved. An additional confined rotational crop study reflecting phenyl-ring labeling must be conducted at 1x the proposed maximum seasonal foliar application rate (0.46 lb ai/A). An acceptable limited field rotational crop study is available; these data will be reevaluated when the outstanding confined rotational crop study is received. In the meantime, the proposed rotational crop restrictions on the submitted labels are deemed appropriate.

Codex maximum residue levels (MRLs) for residues of difenoconazole *per se* have been established at 0.2 ppm for carrot; 0.02 ppm for soya bean (dry); 0.2 ppm for cherries and plums (including prunes); and 0.5 ppm for nectarines and peaches. Canadian and Mexican MRLs have been established for difenoconazole; however, no MRLs have been established for the requested crops. Codex MRLs for residues of difenoconazole and its metabolite CGA-205375, expressed as difenoconazole have been established at 0.2 ppm for edible offal (mammalian) and 0.01 for eggs. Also, Canadian MRLs have been established for difenoconazole at 0.05 ppm for meat byproducts of cattle, goats, hogs, and sheep and at 0.05 ppm in eggs. Based on the submitted/available magnitude of the residue data, harmonization with established Codex MRLs is not possible for carrots, soya bean (dry), cherries, plums (including prunes), nectarines, peaches, edible offal (mammalian), and eggs because the Codex MRLs are too low. Harmonization with the established Canadian MRLs for eggs and meat byproducts of cattle, goats, hogs, and sheep is not possible due to differences in the tolerance expression. Also based on the available magnitude of the residue data, harmonization with established Canadian MRLs is not possible for meat byproducts of cattle, goats, hops, and sheep because the Canadian MRLs are too low.

Regulatory Recommendations and Residue Chemistry Deficiencies

HED has examined the residue chemistry database for difenoconazole. With regards to difenoconazole, pending submission of a revised Section B (see requirements under Directions for Use) and a revised Section F (see requirements under Proposed Tolerances), there are no residue chemistry issues that would preclude granting a conditional registration for the requested uses of the EC, SC, and EW formulations of difenoconazole or establishment of tolerances for residues of difenoconazole only in/on the following commodities:

Aspirated grain fractions..95 ppm
Carrot ....0.50 ppm
Chickpea ....0.08 ppm
Fruit, stone, group 12 ....2.5 ppm
Soybean, hulls..0.20 ppm
Soybean, seed...0.15 ppm
Strawberry..2.5 ppm
Turnip greens ....35 ppm

Furthermore, with the addition of new livestock feedstuffs with this petition, HED concludes that the currently established livestock tolerances for milk, meat, fat, and meat byproducts (except liver) are adequate to support the proposed uses; however, HED recommends increasing the permanent tolerances for residues of difenoconazole and its metabolite, CGA-205375 [1-[2-chloro-4-(4-chloro-phenoxy)phenyl]-2-[1,2,4]triazol-1-yl-ethanol] in liver of cattle, goat, hog, horse, and sheep from 0.20 ppm to 0.40 ppm.

Cattle, liver...0.40 ppm
Goat, liver..0.40 ppm
Hog, liver...0.40 ppm
Horse, liver...0.40 ppm
Sheep, liver...0.40 ppm

Furthermore, due to the lower limits of quantitation (LOQs) of the current livestock enforcement method, HED recommends lowering the permanent tolerance for residues of difenoconazole and its metabolite, CGA-205375 [1-[2-chloro-4-(4-chloro-phenoxy)phenyl]-2-[1,2,4]triazol-1-yl-ethanol] in egg from 0.10 ppm to 0.02 ppm.

Egg..0.02 ppm

A human health risk assessment is forthcoming.

Notes to PM: The current tolerance expression for difenoconazole residues of concern in/on raw agricultural commodities listed under 40 CFR §180.475(a)(1) is consistent with HED's Interim Guidance on Tolerance Expressions (5/27/09, S. Knizner); however, the current tolerance expression for difenoconazole residues of concern in livestock commodities listed under 40 CFR §180.475(a)(2) should be revised to state:

> "Tolerances are established for residues of difenoconazole, including its metabolites and degradates, in the commodities in the following table. Compliance with the tolerance levels specified below is to be determined by measuring the sum of difenoconazole, 1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole, and its metabolite, CGA-205375, 1-[2-chloro-4-(4-chloro-phenoxy)phenyl]-2-[1,2,4]triazol-1-yl-ethanol, calculated as the stoichiometric equivalent of difenoconazole, in the following commodities:"

860.1200 Directions for Use – Pertains to Difenoconazole only

- For chickpeas, the proposed 7-day minimum retreatment interval is not supported by the residue data. Section B and labels for the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 1.05 lb/gal MAI SC formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313), and the 0.73 lb/gal MAI EW formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317) must be revised to specify a minimum retreatment interval of 14 days for chickpeas.

- For soybeans, the proposed 0.46 lb ai/A maximum seasonal application rate is not supported by the residue data. Section B and labels for the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 2.08 lb/gal MAI EC formulation with propiconazole (Inspire™ XT Fungicide; EPA Reg. No. 100-1312), and the 1.05 lb/gal MAI SC formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313) must be revised to specify a maximum seasonal application rate of 0.22 lb ai/A. Furthermore, for clarity, Section B and these labels must be revise to specify the following restriction: "Do not feed soybean hay, forage, or silage to livestock and do not allow grazing of the fields by livestock."

- For strawberries, there appears to be a typographical error on the submitted label for Quadris Top™ Fungicide (EPA Reg. No. 100-1313), the use rate is listed as 8-4 fl. oz. product/A and should be **8-14** fl. oz. product/A.

- Turnip greens should be added to the list of Brassica leafy vegetables specified on the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 1.05 lb/gal MAI SC formulation with azoxytrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313), and the 0.73 lb/gal MAI EW formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317).

- Concerning rotational crop restrictions, okra must be removed from the list of crops on the Quadris Top™ Fungicide Label (EPA Reg. No. 100-1313) permitting a 0-day plantback interval (PBI). There is no individual tolerance for residues of difenoconazole in/on okra (which is considered a miscellaneous commodity) and the currently established tolerance in/on Vegetable, fruiting, group 8 does not include okra. Note: Vegetable, fruiting, group 8-10 does include okra.

<u>860.1550 Proposed Tolerances</u>

- The proposed tolerances should be revised to reflect the recommended tolerance levels and correct commodity definitions as specified in Table 16.

HED recommends that conditional registrations for the requested uses of the EC formulations of difenoconazole, may be converted to unconditional registrations upon submission of the following residue chemistry data:

<u>860.1380 Storage Stability</u>

- Supporting storage stability data for the triazole metabolites are required to support the storage conditions (frozen) and intervals (up to 15 months) of raw agricultural and processed commodity samples collected for the studies reviewed herein. The U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (D363016) and these data are expected to satisfy storage stability data requirements for the subject petition.

- Supporting storage stability data for residues of 1,2,4-triazole (1,2,4-T) are required to support the storage conditions (frozen) and intervals (up to 10 months) of livestock commodity samples collected for the cattle and poultry feeding studies re-evaluated herein. However, storage stability data for these compounds has been requested as part of the Human Health Aggregate Risk Assessment for the triazole metabolites (M.Doherty, *et al.*, 2/7/06) and these data, when submitted, are expected to satisfy storage stability data requirements for the subject petition.

860.1850 Confined Accumulation in Rotational Crops

- The requirement for an additional confined rotational crop study that was previously identified in DP# 344680 (11/5/07, M. Sahafeyan) is a requirement for unconditional registration for this action. A confined rotational crop study reflecting phenyl-ring labeling must be conducted at 1x the proposed maximum seasonal foliar application rate (0.46 lb ai/A). Syngenta Crop Protection, Inc. has submitted a confined rotational crop study (MRID 48203402) which is currently under review in HED (D382946).

In addition to satisfying the conditions of registration specified above for the EC formulations, HED recommends that the conditional registration for the requested uses of the EW formulation of difenoconazole may be converted to an unconditional registration upon submission of the following residue chemistry data:

860.1500 Crop Field Trials

- As recommended by ChemSAC (meeting 01/27/2010), additional side-by-side field trials on grapes comparing difenoconazole residues resulting from applications of the EC and EW formulations should provide a more complete and robust dataset to serve as a surrogate for potential residual differences in/on fruits and vegetables at issue. HED recommends three side-by-side trials on grapes comparing the EC and EW formulations using ground equipment conducted at the maximum use rate on grapes (5 applications at 0.12 lb ai/A/application with a 6-day RTI), or at a slightly exaggerated rate (up to 1.25x or 0.15 lb ai/A/application), and collecting 2-4 samples at several intervals between 0- and 21-days after the last application (DALA). We note that additional grape field trial data were previously required (DP#s 361054 and 362648, B. Cropp-Kohlligian, 9/17/09) to support a proposed use of the 2.82 lb/gal EW formulation of difenoconazole/cyprodinil, Inspire Super™ Fungicide (EPA Reg. No. 100-1317), and the recommended side-by-side grape field trials could be conducted in conjunction with that study.

In addition to satisfying the conditions of registration specified above for the EC formulations, HED recommends that the conditional registration for the requested uses of the SC formulation of difenoconazole may be converted to an unconditional registration upon submission of the following residue chemistry data:

860.1500 Crop Field Trials

- Additional soybean field trials conducted with the SC formulation at the maximum proposed use rate are required. These data may be field trials conducted with a 25% reduction in number or in the form of limited side-by-side trials (conducted at exaggerated rates) to compare residues resulting from the use of an EC formulation with that of the SC formulation.

Background

The chemical structure and nomenclature of difenoconazole and its regulated livestock metabolite CGA-205375, and the physicochemical properties of the technical grade of difenoconazole are presented in Tables 1 and 2.

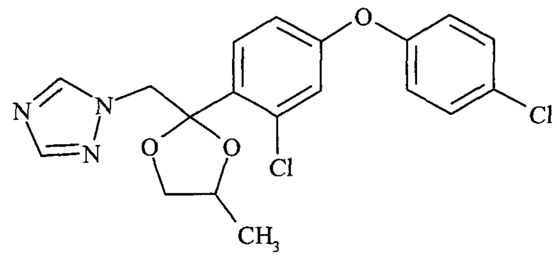
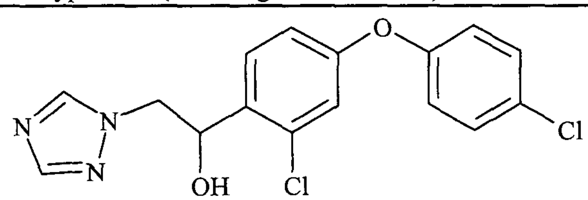
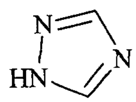
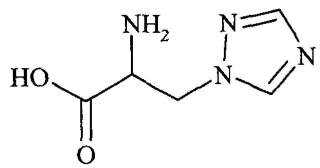
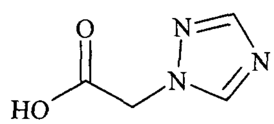
Table 1. Difenoconazole Nomenclature.	
Chemical structure	
Common name	Difenoconazole
Company experimental name	CGA-169374
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CAS registry number	119446-68-3
End-use products (EP)	Inspire™, 2.08 lb/gal EC (EPA Reg. No. 100-1262); Inspire™ XT Fungicide, 2.08 lb/gal MAI EC formulation with propiconazole (EPA Reg. No. 100-1312); Quadris Top™ Fungicide, 1.05 lb/gal MAI SC formulation with azoxystrobin (EPA Reg. No. 100-1313); and Inspire Super™ Fungicide, 0.73 lb/gal MAI EW formulation with cyprodinil (EPA Reg. No. 100-1317).
Chemical structure of CGA-205375 livestock metabolite	
Chemical structure of 1,2,4-Triazole (1,2,4-T)	
Chemical structure of Triazolylalanine (TA)	
Chemical structure of Triazolylacetic acid (TAA)	

Table 2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	
Solvent solubility	g/100 mL at 25 °C: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5 x 10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, $Log(K_{OW})$	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

860.1200 Directions for Use

Syngenta Crop Protection, Inc. has submitted a Section B reflecting directions for use for the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262) on carrots, chickpeas, soybeans, stone fruits and strawberries; supporting draft labeling was also submitted. In addition, Syngenta Crop Protection, Inc. is proposing to add some or all of the proposed uses to the following multiple active ingredient (MAI) products and has submitted supporting draft labeling for each product: a 2.08 lb/gal MAI EC formulation with propiconazole (Inspire™ XT Fungicide; EPA Reg. No. 100-1312); a 1.05 lb/gal MAI SC formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313); and a 0.73 lb/gal MAI EW formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317). The subject end-use products are identified in Table 3, and the use directions are summarized in Table 4.

Table 3.	**Summary of Proposed End-Use Products.**				
Trade Name	EPA Reg. No.	ai Content	Formulation Type	Target Crops Relevant to PP#9F7676	Label Date
Inspire™ Fungicide	100-1262	Difenoconazole 2.08 lb/gal (23.2%)	Emulsifiable concentrate (EC)	Carrots, chickpeas, soybeans, stone fruits, and strawberries.	12/13/10
Inspire™ XT Fungicide	100-1312	Difenoconazole 2.08 lb/gal (22.8%) Propiconazole 2.08 lb/gal (22.8%)	EC	Carrots, soybeans, stone fruits, and strawberries.	1/6/11
Quadris Top™ Fungicide	100-1313	Difenoconazole 1.05 lb/gal (11.4%) Azoxystrobin 1.67 lb/gal (18.2%)	Suspension concentrate (SC)	Carrots, chickpeas, soybeans, stone fruits, and strawberries.	1/6/11
Inspire Super™ Fungicide	100-1317	Difenoconazole 0.73 lb/gal (8.4%) Cyprodinil 2.09 lb/gal (24.1%)	Emulsion oil in water (EW)	Carrots, chickpeas, stone fruits, and strawberries.	12/17/09

Table 4. Summary of Directions for Use of Difenoconazole.

Appl. Timing, Type, and Equip.[1]	Formulation [EPA Reg. No.]	Appl. Rate (lb ai/A)	Max. No. Appl. per Season	Max. Seasonal Appl. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations[1,2]
Carrots						
Foliar, Broadcast, Ground (≥15 gal/A), aerial (≥10 gal/A) or chemigation	2.08 lb/gal EC [100-1262]	0.09-0.114	Not specified (NS)	0.46	7	For treatment of Cercospora leaf spot, Alternaria leaf blight, and Powdery mildew. Applications to begin prior to disease onset (all). No more than 2 consecutive applications to be made before alternating with a different mode of action (MOA) fungicide. A 7- to 10-day RTI is specified.
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (≥10 gal/A)	2.08 lb/gal MAI EC [100-1312]				14	
Foliar, Broadcast, Ground (≥15 gal/A), aerial (≥10 gal/A) or chemigation	1.05 lb/gal MAI SC [100-1313]	0.07-0.12			7	Same as for 100-1262 except: Also for treatment of Southern blight.
Foliar, Broadcast, Ground only (≥15 gal/A)	0.73 lb/gal MAI EW [100-1317]	0.08-0.114			7	Same as for 100-1262 except: Label prohibits feeding leaves of carrots to cattle or other livestock.
Chickpeas						
Foliar, Broadcast, Ground (≥15 gal/A), aerial (gal/A not specified[1]) or chemigation	2.08 lb/gal EC [100-1262]	0.09-0.114	NS	0.46	14	For treatment of Altenaria blight, Ascochyta blight, Powdery mildew and Rust. Applications to begin prior to disease onset (all). No more than 2 consecutive applications to be made before alternating with a different mode of action (MOA) fungicide. A 7- to 10-day RTI is specified.
	1.05 lb/gal MAI SC [100-1313]	0.07-0.12				
Foliar, Broadcast, Ground only (≥15 gal/A)	0.73 lb/gal MAI EW [100-1317]	0.08-0.114				Same as for 100-1262 except: Also for treatment of Gray mold.

Table 4. Summary of Directions for Use of Difenoconazole.

Appl. Timing, Type, and Equip.[1]	Formulation [EPA Reg. No.]	Appl. Rate (lb ai/A)	Max. No. Appl. per Season	Max. Seasonal Appl. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations[1,2]
Soybeans						
Foliar, Broadcast, Ground (gal/A not specified[1]), aerial (≥2 gal/A) or chemigation	2.08 lb/gal EC [100-1262]	0.09-0.114	NS	0.46	14	For treatment of Anthracnose, Altenaria leaf spot, Brown spot, Cercospora blight and leaf spot, Frogeye leaf spot, Pod and stem blight, and Powdery mildew. Applications to begin prior to disease onset (all). No more than 2 consecutive applications to be made before alternating with a different mode of action (MOA) fungicide. A 7- to 10-day RTI is specified. **The label prohibits feeding soybean hay, forage and silage.**
Foliar, Broadcast, Ground (gal/A not specified[1]) or aerial (≥2 gal/A)	2.08 lb/gal MAI EC [100-1312]	0.09-0.114				Same as for 100-1262 except: Also for treatment of Soybean rust. A 14- to 21-day RTI is specified. May be applied up to Stage R6 or within 14 days of harvest, whichever is longer. Addition of an oil-based additive is recommended for improved coverage and penetration when applying by air.
Foliar, Broadcast, Ground (gal/A not specified[1]), aerial (≥2 gal/A) or chemigation	1.05 lb/gal MAI SC [100-1313]	0.07-0.12				Same as for 100-1262.

Table 4. Summary of Directions for Use of Difenoconazole.

Appl. Timing, Type, and Equip.[1]	Formulation [EPA Reg. No.]	Appl. Rate (lb ai/A)	Max. No. Appl. per Season	Max. Seasonal Appl. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations[1,2]
Stone fruits: apricots, sweet cherries, tart cherries, nectarines, peaches, plums, plumcot, and prunes.						
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (≥10 gal/A)	2.08 lb/gal EC [100-1262]	0.09-0.114	NS	0.46	0	For treatment of Brown rot blossom blight, begin applications at early bloom and continue through petal fall. For Brown rot on fruit, apply as needed a maximum of two sprays during the preharvest period up to the day of harvest (minimum of a 7-day retreatment interval). For treatment of Scab, Alternaria spot and fruit rot, Anthracnose, Leaf rust, Powdery mildew, and Shot hole, follow the Brown rot blossom blight schedule. Make additional applications on a 10-to 14-day interval from the end of petal fall to harvest.
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (≥10 gal/A)	2.08 lb/gal MAI EC [100-1312]	0.09-0.114				
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (≥10 gal/A)	1.05 lb/gal MAI SC [100-1313]	0.07-0.12				
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (≥10 gal/A)	0.73 lb/gal MAI EW [100-1317]	0.08-0.114			2	Same as for 100-1262 except: Aerial application is allowed in CA only: 1 Application, with additional applications by ground equipment. Do not apply to sweet cherries.

Table 4. Summary of Directions for Use of Difenoconazole.

Appl. Timing, Type, and Equip.[1]	Formulation [EPA Reg. No.]	Appl. Rate (lb ai/A)	Max. No. Appl. per Season	Max. Seasonal Appl. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations[1,2]
Strawberries						
Foliar, Broadcast, Ground (≥15 gal/A), aerial (≥10 gal/A) or chemigation	2.08 lb/gal EC [100-1262]	0.09-0.114	NS	0.46	0	For treatment of Anthracnose, Leaf spot, Powdery mildew, and Leaf rust. Applications to begin prior to disease onset (all). No more than 2 consecutive applications to be made before alternation with a different MOA fungicide. A 7- to 14-day RTI is specified.
	2.08 lb/gal MAI EC [100-1312]	0.09-0.114				
	1.05 lb/gal MAI SC [100-1313][2]	0.07-0.12				
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (≥10 gal/A)	0.73 lb/gal MAI EW [100-1317]	0.08-0.114				Same as for 100-1262 except: Aerial application is allowed in CA only: 1 application, with additional applications by ground equipment.

PHI = preharvest interval RTI = retreatment interval.

1 With regards to the crops under consideration, under general directions, all labels indicated that, if not specified otherwise, ground and aerial applications were to be made in a minimum of 10-15 gal/A and 5 gal/A, respectively. The use of ground and aerial ULV spray systems are prohibited for the SC product formulation (EPA Reg. No. 100-1313) and the EW product formulation (EPA Reg. No. 100-1317). Note: Ultra-low volume uses = <10 gal/A for orchards and <2 gal/A for all other crops

2 There appears to be a typographical error on the submitted label, the use rate is listed as 8-4 fl. oz. product/A and should be **8-14** fl. oz. product/A.

The EC product formulations (EPA Reg. Nos. 100-1262 and 100-1312) are proposed for multiple foliar applications at 0.09-0.114 lb ai/A/application for maximum seasonal rates of 0.46 lb ai/A on carrots, chickpeas (excluding EPA Reg. No. 100-1312), soybeans, stone fruit, and strawberries. The proposed preharvest intervals (PHIs) are 7 days for carrots (14 days for EPA Reg. No. 100-1312), 14 days for chickpeas and soybeans, and 0 days for stone fruit and strawberries. The SC formulation product (EPA Reg. No. 100-1313) and the EW formulation product (EPA Reg. No. 100-1317) are proposed for the same crops, with the except of the EW formulation which is not proposed for use on soybeans, with essentially the same use patterns and the same minimum PHIs or, in the case of the proposed use of the EW formulation on stone fruits, a slightly more restrictive PHI. There is a proposed restriction against the feeding of soybean hay, forage and silage which is considered to be under grower control.

None of the proposed labels lists turnip greens as a separate use site; however, the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 1.05 lb/gal MAI SC formulation with azoxytrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313), and the 0.73 lb/gal MAI EW formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317) include use directions for Brassica leafy vegetables; however, none of the proposed labels lists turnip greens as a commodity under Brassica leafy vegetables.

The following rotational crop restrictions are specified for listed products:

- For the 2.08 lb/gal difenoconazole EC formulation (EPA Reg. No. 100-1262): 0-day plantback interval (PBI) for cucurbit vegetables, Brassica (Cole) leafy vegetables, bulb vegetables, tomatoes, fruiting vegetables, potatoes, tuberous and corm vegetables, sugar beets, canola, cereals (wheat, barley, and triticale), cotton, and sweet corn; and 8-month PBI for all other crops intended for food and feed.
- For the 2.08 lb/gal MAI EC formulation with propiconazole (EPA Reg. No. 100-1312): 0-day PBI for bulb vegetables, carrots, cereals (wheat, barley, and triticale), soybeans, strawberry, sugar beets, and sweet corn; and 8-month PBI for all other crops unless the crop appears on the label.
- For the 1.05 lb/gal MAI SC formulation with azoxystrobin (EPA Reg. No. 100-1313): 0-day PBI for Brassica (Cole) leafy vegetables, bulb vegetables, canola, carrots, cereals (wheat, barley, and triticale), chickpea, cotton, cucurbit vegetables, eggplant, okra, pepper, potatoes, soybeans, strawberries, sweet corn, tomatoes, and tuberous & corm vegetable subgroup; 36-day PBI for sugar beets; 12-month PBI for buckwheat, millet, oats, and rye; and an 8-month PBI for all other crops intended for food and feed.
- For the 0.73 lb/gal MAI EW formulation with cyprodinil (EPA Reg. No. 100-1317): 0-day PBI for Brassica (Cole) leafy vegetables, bulb vegetables, carrots, chickpea, citrus, cucurbit vegetables, strawberries, and tomatoes; 30-day PBI for canola, cereals (wheat, barley, and triticale), cotton, fruiting vegetables, potatoes, sugar beets, sweet corn, and tuberous & corm vegetables; and 8-month PBI for all other crops intended for food and feed.

Conclusions. The proposed use directions are adequate to allow evaluation of the residue data relative to the proposed uses of difenoconazole. The available field trial data reflect the proposed use patterns for all of the submitted field trials except as noted below.

For chickpeas, the proposed 7-day minimum retreatment interval is not supported by the residue data. Section B and labels for the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 1.05 lb/gal MAI SC formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313), and the 0.73 lb/gal MAI EW formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317) must be revised to specify a minimum retreatment interval of 14 days for chickpeas.

For soybeans, the proposed 0.46 lb ai/A maximum seasonal application rate is not supported by the residue data. Section B and labels for the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 2.08 lb/gal MAI EC formulation with propiconazole (Inspire™ XT Fungicide; EPA Reg. No. 100-1312), and the 1.05 lb/gal MAI SC formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313) must be revised to specify a maximum seasonal application rate of 0.22 lb ai/A. Furthermore, for clarity, Section B and these labels must be revise to specify the following restriction: "Do not feed soybean hay, forage, or silage to livestock and do not allow grazing of the fields by livestock."

For strawberries, there appears to be a typographical error on the submitted label for Quadris Top™ Fungicide (EPA Reg. No. 100-1313), the use rate is listed as 8-4 fl. oz. product/A and should be **8-14** fl. oz. product/A.

Turnip greens should be added to the list of Brassica leafy vegetables specified on the 2.08 lb/gal EC formulation (Inspire™ Fungicide; EPA Reg. No. 100-1262), the 1.05 lb/gal MAI SC formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313), and the 0.73 lb/gal MAI EW formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317).

Concerning rotational crop restrictions, okra must be removed from the list of crops on the Quadris Top™ Fungicide Label (EPA Reg. No. 100-1313) permitting a 0-day plantback interval (PBI). There is no individual tolerance for residues of difenoconazole in/on okra (which is considered a miscellaneous commodity) and the currently established tolerance in/on Vegetable, fruiting, group 8 does not include okra. Note: Vegetable, fruiting, group 8-10 does include okra.

860.1300 Nature of the Residue - Plants

Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan
MARC Decision Memo, 7/22/94, G. Kramer

The nature of the residue in plants is understood based on acceptable plant metabolism studies reflecting foliar applications in canola, grape, potato, tomato, and wheat and seed treatment in wheat. Based on the results of available plant metabolism studies, the petitioner has proposed that difenoconazole is metabolized in plants by the hydroxylation of the phenyl ring and/or cleavage of the dioxolane ring followed by cleavage of the carbon-carbon bridge between the phenyl and triazole rings.

Previously, when the first foliar uses of difenoconazole on crop commodities were proposed (DP# 340379), HED re-evaluated the available plant metabolism data to determine if residues other than difenoconazole needed to be included in the tolerance expression and/or the risk assessment and concluded that the residue of concern was difenoconazole *per se* for both tolerance enforcement and risk assessment for the crops (fruiting vegetables, pome fruits, sugar beets, tuberous and corm vegetables, and imported papaya) in the petition (PP#6F7115) under consideration. In keeping with the previous decision, HED concludes that the residue of concern for both tolerance enforcement and risk assessment for the crops included in this petition is difenoconazole *per se*.

860.1300 Nature of the Residue - Livestock

Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan
MARC Decision Memo, 7/22/94, G. Kramer
Residue Chemistry Memo DP#s 203644 and 203645, 6/16/94, G. Kramer
Residue Chemistry Memo DP#s 172067 and 178394, 10/26/92, R. Lascola

The nature of the residue in livestock is understood based on acceptable goat and hen metabolism studies. The data were originally evaluated in support of seed treatment uses only, and HED concluded that the residue of concern in livestock commodities was difenoconazole *per se*. When the first foliar uses of difenoconazole on crop commodities were proposed (DP# 340379), HED re-evaluated the livestock metabolism data and concluded that the residues of concern for both tolerance setting and risk assessment for livestock commodities are difenoconazole and its metabolite CGA-205375.

860.1340 Residue Analytical Methods

Crop Commodities
Residue Chemistry Memo DP# 356135, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

Enforcement methods: An adequate enforcement method, GC/NPD method AG-575B, is available for the determination of residues of difenoconazole *per se* in/on plant commodities. An adequate enforcement method, GC/MSD method AG-676A, is also available for the determination of residues of difenoconazole *per se* in/on canola and barley commodities. A confirmatory method, GC/MSD method AG-676, is also available. The LOQs are 0.01-0.05 ppm.

Data collection methods - difenoconazole: Samples from the carrot, chickpea, soybean, stone fruit, and strawberries crop field trial and the plum and soybean processing studies were analyzed for residues of difenoconazole using an LC/MS/MS method, Syngenta REM 147.08. This method has been reviewed previously (DP# 340379).

Briefly, residues of difenoconazole were extracted from crop matrices using methanol:concentrated ammonium hydroxide (80:20, v:v) via heating at reflux. An aliquot of the extract was diluted to volume with water and cleaned up by solid-phase extraction (SPE; Oasis™ HLB cartridge). Residues of difenoconazole were determined by LC/MS/MS analysis.

The LOQ was 0.01 ppm for difenoconazole in each crop commodity. The method was adequate based on acceptable concurrent recovery data. The fortification levels used in concurrent method recovery were adequate to bracket expected residues in all commodities.

Data collection methods - TA, TAA, and 1,2,4-T: Samples from the carrot, chickpea, soybean, stone fruit, and strawberry crop field trial and the plum and soybean processing studies were analyzed for residues of the triazole metabolites using Morse Laboratories LC/MS/MS method Meth-160, Revision #2. This method has been reviewed previously (DP# 340379).

Briefly, residues of TA, TAA, and 1,2,4-T were extracted using methanol:water (80:20, v:v); the extract was isolated by filtration and brought to volume using methanol:water (80:20, v:v). [Orange oil samples were first diluted with hexane then extracted twice with methanol/water; extracts were combined and brought to volume with methanol/water.] Aliquots of the extract were then processed separately through SPE cleanup and/or derivatization steps which were specific for each analyte. Internal standard, specific for each analyte, was added to each aliquot prior to processing. The 1,2,4-T aliquot did not undergo cleanup and was directly derivatized with dansyl chloride to produce the dansyl derivative, which was partitioned into ethyl acetate; the ethyl acetate fraction was evaporated to dryness and redissolved in acetonitrile (ACN):water (30:70, v:v) for analysis. The TA aliquot was derivatized to the butyl ester using HCl/butanol and then further derivatized using HFBA (heptafluorobutyric anhydride). The TAA aliquot was purified through a C-18 SPE cartridge, then derivatized using HCl/butanol esterification. The TA and TAA derivatized extracts were evaporated to dryness and redissolved in ACN:water (30:70, v:v) for analysis. Determination and quantitation of derivatives of 1,2,4-T, TA, and TAA were conducted using LC/MS/MS; results were reported in terms of the original triazole metabolite.

The LOQ was 0.01 ppm for each analyte in each crop commodity. The method was adequate based on acceptable concurrent recovery data. The fortification levels used in concurrent method recovery were adequate to bracket expected residues in all commodities.

Conclusions. The submitted and available data are adequate to satisfy data requirements for residue analytical methods for crop commodities. An adequate tolerance enforcement method is available for determination of residues of difenoconazole *per se*, and samples from the crop field trial and processing studies were analyzed for residues of difenoconazole and the triazole metabolites TA, TAA, and 1,2,4-T using acceptable methods.

Livestock Commodities
Analytical Chemistry Branch Memo, 10/29/07, C. Stafford
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan
Residue Chemistry Memo DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 374898, 3/3/10, B. Cropp-Kohlligian

Enforcement methods: An acceptable enforcement method, GC/NPD Method AG-544A, was previously submitted for the determination of residues of difenoconazole *per se* in livestock commodities. The method was validated by the Agency; however, it does not determine residues of CGA-205375, and thus is not adequate as a tolerance enforcement method.

An LC/MS/MS method, identified as Method REM 147.07, was previously submitted under PP#6F7115 (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan) for the determination of residues of difenoconazole and CGA-205375 in livestock commodities. The method LOQs are 0.01 ppm for livestock tissues and 0.005 ppm for milk. HED tentatively concluded that Method REM 147.07 would be suitable for enforcement purposes pending submission of the following: (1) additional information from the ILV of the method; (2) revision of the method to correct all references to "crop matrices"; (3) confirmatory analysis procedures for the method; and (4) successful Agency method validation. HED subsequently reassessed the need for additional information from the ILV of the method and concluded that this information is not needed based on the method validation conducted by the Analytical Chemistry Branch (ACB memo from C. Stafford, ACB Project # B07-26, dated 10/29/07) which found that the ILV study data submitted for Method REM 147.07 (MRID 46950221) are acceptable and indicate that the method performance is reproducible.

Method REM 147.07 has been reviewed by the ACB (ACB memo from C. Stafford, ACB Project # B07-26, dated 10/29/07). ACB found the method to be adequate for tolerance enforcement without a laboratory trial but noted that confirmatory requirements were not met because only one MS/MS ion transition was documented for each analyte. ACB recommended that the petitioner provide information for a second MS/MS ion transition for each analyte, or provide an alternate chromatographic column and/or mobile phase combination.

In response, Syngenta Crop Protection, Inc. previously submitted a revised version of Method REM 147.07, identified as Method REM 147.07b, as well as a confirmatory HPLC/UV method, identified as Method REM 147.06, for the determination of residues of CGA-205375 in/on livestock commodities (DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian). Method REM 147.07b is identical to the original version of the method, except that references to "crop matrices" have been removed; the recommendation to include a second MS/MS ion transition was not addressed. A complete description of confirmatory Method REM 147.06 and adequate supporting method validation data using samples of muscle, liver, kidney, fat, milk, and eggs fortified at the LOQ and 10x the LOQ (0.010 ppm and 0.10 ppm for tissues and egg, and 0.005 and 0.050 ppm for milk) were submitted.

Conclusions. The available data are adequate to satisfy data requirements for residue analytical methods for livestock commodities. The LC/MS/MS method identified as Method REM 147.07b is acceptable for the enforcement of tolerances for residues of difenoconazole and CGA-205375 in livestock commodities; the method LOQs are 0.01 ppm for livestock tissues and 0.005 ppm for milk. [Note: The LOQs of the current livestock tolerance enforcement method (0.01 ppm) are lower than the previous enforcement method(s).] The GC/NPD method identified as Method AG-544A is an acceptable confirmatory method for the determination of residues of difenoconazole in livestock commodities. The HPLC/UV method identified as Method REM 147.06 is an acceptable confirmatory method for the determination of residues of CGA-205375 in livestock commodities. These methods have been forwarded to FDA for inclusion in the PAM Volume II and to USDA, FSIS.

860.1360 Multiresidue Methods
Residue Chemistry Memo DP#s 172067 and 178394, 10/26/92, R. Lascola
Email from C. Stafford (Analytical Chemistry Branch) to B. Cropp-Kohlligian dated 9/2/09

Multiresidue methods (MRM) testing data (MRID 42090054) were previously submitted in conjunction with PP#2E4051 (DP#s 172067 and 178394, 10/26/92, R. Lascola). The study investigated the recovery of difenoconazole and its metabolites CGA-205374, CGA-205375, and CGA-189138 through the MRM methods of PAM Vol. I. Based on the study results, HED concluded, as did the petitioner, that the MRM methods were not likely to be appropriate for determining residues of difenoconazole and its related compounds in plant and livestock tissues. The study was forwarded to FDA for further review. Difenoconazole is not listed in the most recent PESTDATA (1999).

In contradiction to the MRM study evidence, Analytical Chemistry Branch (ACB) has noted (Email from C. Stafford (ACB) to B. Cropp-Kohlligian dated 9/2/09) that (1) FDA routinely monitors for difenoconazole by GC/MS using their current modified Luke procedures which are not in the published PAM I manual; (2) difenoconazole has also been tested through the QuEChERS (Quick, Easy, Cheap, Effective, Rugged, and Safe) method which is just beginning to be implemented in the FDA field labs using LC/MS/MS; and (3) the USDA-PDP program labs monitor for difenoconazole; the California Department of Food and Agriculture (CDFA), a participating laboratory, uses a multiresidue method with LC/MS analysis. Based on these facts, HED accepts that difenoconazole is recoverable through existing multiresidue methods, although the evidence is non-guideline and a conclusion concerning whether recovery is complete (>80%) cannot be reached. No additional MRM testing data are required at this time.

860.1380 Storage Stability

Crop Commodities

Residue Chemistry Memo DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 356135, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

No supporting storage stability data for difenoconazole *per se* and/or its metabolites in/on crop commodities were provided in the subject submissions to support the new field trial and processing studies.

Adequate storage stability data are available indicating that residues of difenoconazole *per se* are stable at -20 °C for at least two years in/on cotton seed, cottonseed oil, and cottonseed meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw. Data are also available indicating that residues of difenoconazole *per se* are stable at -20 °C for at least one year in/on banana, lettuce, and soybean seed.

These data represent sufficiently diverse crops (a leafy vegetable, a fruit, a root crop, a non-oily grain, and an oilseed) to allow translation of storage stability data for residues of difenoconazole *per se* to all raw agricultural crop commodities (RACs) for a one-year storage interval, when stored under frozen conditions. The available storage stability data for the two-year storage interval are not sufficient to allow translation to all RACs because no data are available for a leafy vegetable. Although the available storage stability data are not sufficiently representative for all processed commodities, which usually requires an oilseed, a fruit/fruiting vegetable, and a non-oily grain, when taken together with the available storage stability data on RAC matrices, they are deemed adequate to demonstrate the stability of residues of difenoconazole *per se* in all processed commodities for up to two years when stored under frozen conditions.

The U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (D363016).

The storage durations and conditions of samples from the crop field trials submitted to support this petition are presented in Table 5.

Table 5. Summary of Storage Conditions and Durations of Samples from the Submitted Crop Field Trial and Processing Studies.

Matrix	Storage Temperature (°C)	Maximum Actual Storage Duration (months)	Interval of Demonstrated Storage Stability
Difenoconazole - Raw Agricultural Commodities			
Carrot (root)	<-10	12.5	None provided with the current submissions; however, based on previously submitted storage stability data, when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable for up to two years in/on cotton seed, potato tuber, tomato, wheat forage, wheat grain, and wheat straw.
Chickpea (seed)		6.0	
Soybean, seed		5.1	
Soybean, forage		6.2	
Soybean, hay		6.3	
Soybean, AGF		10.4	
Cherry		14.5	
Peach		5.2	
Plum		14.0	
Strawberry		8.2	
Difenoconazole - Processed Commodities			
Soybean, AGF	<-10	10.4	None provided with the current submissions; however, based on previously submitted storage stability data, when stored under frozen conditions, residues of difenoconazole *per se* are stable for up to two years in/on cottonseed oil and meal; tomato paste and puree; and sugar beet sugar, dried pulp, and molasses. Taken together with the available RAC storage stability data discussed above, residues of difenoconazole *per se* in/on all processed commodities are expected to be stable for up to two years, when stored under frozen conditions.
Soybean, meal		3.2	
Soybean, hulls		5.5	
Soybean, oil, refined		3.2	
Prunes		14.2	
1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolyl acetic acid (TAA) - Raw Agricultural Commodities			
Carrot (root)	<-10	11.7	None provided with the current submissions; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (D363016).
Chickpea (seed)		5.2	
Soybean, seed		5.4	
Soybean, forage		5.6	
Soybean, hay		6.9	
Soybean, AGF		10.1	
Cherry		15.0	
Peach		13.2	
Plum		4.9	
Strawberry		8.2	
1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolyl acetic acid (TAA) - Processed Commodities			
Soybean, AGF	<-10	10.1	*See Raw Agricultural Commodities above.*
Soybean, meal		4.2	
Soybean, hulls		4.9	
Soybean, oil, refined		4.1	
Prunes		14.2	

Conclusions. No new storage stability data for difenoconazole *per se* in/on raw agricultural crop and processed commodities were provided in the subject submissions. Samples of raw agricultural commodities from the submitted crop field trial were stored frozen for less than 12 months prior to analysis for difenoconazole *per se*, except for samples of carrot, cherry, and plum, which were stored for up to 14.5 months prior to analysis. Available storage stability data represent sufficiently diverse crops (a leafy vegetable, a fruit, a root crop, a non-oily grain, and an oilseed) to allow translation of storage stability data for residues of difenoconazole *per se* to all raw agricultural crop commodities (RACs) for a one-year storage interval, when stored under frozen conditions. Available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on potato tuber are adequate to support the storage intervals and conditions for carrot samples reviewed herein. Available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on tomato are adequate to support the storage intervals and conditions for cherry and plum samples reviewed herein. Samples of soybean meal, soybean hulls, soybean refined oil, soybean AGF, and prunes collected from processing studies were stored frozen for less than 15 months prior to analysis for difenoconazole *per se*. Available storage stability data for residues of difenoconazole *per se* in/on various processed commodities, when taken together with the available RAC storage stability data , are adequate to support the storage intervals and conditions of samples collected from the soybean and plum processing studies reviewed herein.

With regards to the triazole metabolites. No new storage stability data for the triazole metabolites 1,2,4-T, TA, and TAA to support the storage conditions and intervals of samples of the raw agricultural or processed commodities addressed herein were provided; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (D363016) and these data are expected to satisfy storage stability data requirements for the subject petition.

Livestock Commodities

Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan
Residue Chemistry Memo DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian
Residue Chemistry Memo DP# 375194, 6/17/10, B. Cropp-Kohlligian

No new meat, milk poultry, and egg data and/or supporting storage stability data for difenoconazole and/or its metabolites in/on livestock commodities were provided in the subject submissions.

Conclusions. With regards to residues of difenoconazole (CGA-169374) and its metabolite CGA-205375, the available storage stability data (47957201.der) and supplemental storage stability information provided in Report Number ABR-93012 (MRID 47957202) and Report Number 202/99 (MRID 47957203) are deemed adequate to support the storage intervals and conditions of samples collected from the cattle and poultry feeding studies previously submitted, reviewed by HED under PP# 6F7115 (D340379, 8/9/07, W. Wassell and M. Sahafeyan), and re-evaluated herein. The information in Report Numbers ABR-93012 and 202/99 is considered supplemental since study details and raw data were not provided.

With regards to the triazole metabolites, supporting storage stability data for residues of 1,2,4-triazole (1,2,4-T) are required to support the storage conditions (frozen) and intervals (up to 10 months) of livestock commodity samples collected for the cattle and poultry feeding studies re-evaluated herein. However, storage stability data for these compounds has been requested as part of the Human Health Aggregate Risk Assessment for the triazole metabolites (M.Doherty, *et al.,* 2/7/06) and these data, when submitted, are expected to satisfy storage stability data requirements for the subject petition.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan
Residue Chemistry Memo DP# 375194, 6/17/10, B. Cropp-Kohlligian

There are several cattle feedstuffs associated with the proposed uses: carrot culls (considered an alternative feedstuff), soybean seed, soybean meal, soybean hulls and soybean aspirated grain fractions (AGF). There are two swine and poultry feedstuffs associated with the proposed uses: soybean seed and soybean meal.

In June 2008, HED issued new guidance concerning the construction of maximum reasonably balanced diets (Table 1 Feedstuffs, October 2006 version). The dietary burdens for livestock are recalculated herein, reflecting the recent guidance, and the proposed/recommended and established tolerances for difenoconazole. The results are presented in Table 6.

The maximum reasonable dietary burdens are recalculated to be: 6.0 ppm for beef cattle, 1.6 ppm for dairy cattle, 0.09 ppm for swine, and 0.11 ppm for poultry. The beef and dairy cattle diets are dominated by contributions from soybean AGF and wet apple pomace (considered an alternative feedstuff), respectively.

Table 6. Calculation of Dietary Burdens of Difenoconazole Residues to Livestock.

Feedstuff [1]	Type[2]	% Dry Matter[3]	% Diet[3]	Established/Recommended Tolerance (ppm)	Dietary Contribution (ppm)[4]
Beef Cattle					
Sugar beet, dried pulp	R	88	15	1.9	0.32
Aspirated Grain Fractions	CC	85	5	95	5.59
Wheat, grain	CC	89	20	0.1	0.02
Barley, grain	CC	88	50	0.1	0.06
Untreated	CC	--	5	--	0.00
Soybean, meal (seed)	PC	92	5	0.15	0.01
TOTAL BURDEN	--	--	100	--	**6.0**

Table 6. Calculation of Dietary Burdens of Difenoconazole Residues to Livestock.

Feedstuff [1]	Type[2]	% Dry Matter[3]	% Diet[3]	Established/Recommended Tolerance (ppm)	Dietary Contribution (ppm)[4]
Dairy Cattle					
Wheat, forage	R	25	10	0.1	0.04
Soybean, hulls	R	90	20	0.20	0.04
Sugar beet, dried pulp	R	88	15	1.9	0.32
Apple, wet pomace	CC	40	10	4.5	1.13
Barley, grain	CC	88	35	0.1	0.04
Soybean, meal (seed)	PC	92	10	0.15	0.02
TOTAL BURDEN	--	--	100	--	**1.6**
Swine					
Wheat, milled byprdts[5]	CC	88	50	0.1[5]	0.050
Barley, grain	CC	88	20	0.1	0.020
Untreated	CC	--	15	--	0.000
Soybean, seed	PC	89	15	0.15	0.022
TOTAL BURDEN	--	--	100	--	**0.09**
Poultry					
Wheat, grain	CC	89	75	0.1	0.075
Soybean, seed	PC	89	20	0.15	0.030
Soybean, meal[6]	PC	92	5	0.15[6]	0.008
TOTAL BURDEN	--	--	100	--	**0.11**

1 According to OPPTS 860.1000 Table 1 Feedstuffs (June 2008), only one of the following alternative feedstuffs is to be included in any theoretical livestock diet: almond hulls, wet apple pomace, aspirated grain fractions, carrot culls, dried citrus pulp, sweet corn cannery waste, cotton gin byproducts, pineapple process residue, and potato processed waste.
2 R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.
3 OPPTS 860.1000 Table 1 Feedstuffs (June 2008).
4 Contribution = ([tolerance/% DM] X % diet) for beef and dairy cattle.
Contribution = (tolerance X % diet) for swine and poultry.
5 Translated from wheat grain.
6 Translated from soybean seed.

Cattle

Syngenta Crop Protection, Inc. previously submitted a cattle feeding study (MRID 46950226) with difenoconazole (MRID 46950226) which was reviewed by HED (PP# 6F7115; D340379, 8/9/07, W. Wassell and M. Sahafeyan). These data are the basis for the established tolerances for residues of difenoconazole and its metabolite CGA-205375 in cattle, goat, hog, horse, and sheep commodities. [Note: Syngenta Crop Protection, Inc. also previously submitted a report of a second cattle feeding study (Report Number 202/99; MRID 47957203) which was reviewed by HED (D375194, 6/17/10, B. Cropp-Kohlligian) and deemed supplemental.]

Three treatment groups of three dairy cows each were dosed orally with gelatin capsules containing difenoconazole at target dose rates of 1, 5, and 15 ppm in the diet (dry-weight basis) for 29-30 consecutive days; actual dose rates were 0.94, 4.24, and 14.26 ppm. The actual dosing rates correspond to 0.2x, 0.7x, and 2.4x the dietary burden for beef cattle and 0.6x, 2.7x, and 8.9x the dietary burden for dairy cattle. Cows were milked twice daily, and samples were composited daily for each cow. One cow from each treatment group was sacrificed on Day 29 and the remaining two cows from each treatment group were sacrificed on Day 30. All cows were sacrificed 20-23 hours after the final dose. Samples of liver, kidney, renal fat, mesenterial fat, subcutaneous fat, round muscle, tenderloin muscle, and diaphragm muscle were collected from each cow. Samples of milk collected on study days 0, 2, 5, 8, 12, 15, 19, 22, 26, and 28 from all dose levels were retained for analysis.

Milk and tissue samples were analyzed for residues of difenoconazole and CGA 205375 using an LC/MS/MS method, REM 147.07 (precursor to the current enforcement Method 147.07b), and for residues of 1,2,4-T using an LC/MS/MS method, RAM 455/01. These methods are adequate for data collection based on acceptable method recoveries. The validated LOQs for REM 147.07, determined as the lower level of method validation (LLMV), were 0.005 ppm for each analyte in milk and 0.01 ppm for each analyte in tissues. The validated LOQ for RAM 455/01, determined as the LLMV, was 0.01 ppm in all matrices. No LODs were reported for either method.

The maximum residues of difenoconazole, CGA 205375, and 1,2,4-T in milk and tissues at each dosing level are presented in Table 7 below.

Table 7. Maximum Residues of Difenoconazole, CGA 205375, and 1,2,4-Triazole in Cattle Milk and Tissues by Feeding Level.

Matrix	Maximum Residues by Feeding Level (ppm)		
	0.94 ppm	4.24 ppm	14.3 ppm
Difenoconazole Residues			
Milk	<0.005	<0.005	<0.005
Fat (renal, mesenterial, and subcutaneous)	<0.01	<0.01	<0.01
Kidney	<0.01	<0.01	<0.01
Liver	<0.01	0.02	0.03
Muscle (round, tenderloin, and diaphragm)	<0.01	<0.01	<0.01
CGA 205375 Residues			
Milk	<0.005	0.007	0.020
Fat, renal	0.01	0.05	0.13
Fat, mesenterial	0.01	0.04	0.14
Fat, subcutaneous	0.02	0.04	0.13
Kidney	0.01	0.04	0.12
Liver	0.07	0.23	0.66
Muscle, round	<0.01	0.01	0.04
Muscle, tenderloin	<0.01	0.01	0.04
Muscle, diaphragm	<0.01	0.01	0.05
1,2,4-Triazole Residues			
Milk	<0.01	0.03	0.05
Fat, renal	<0.01	<0.01	<0.01
Fat, mesenterial	<0.01	<0.01	<0.01
Fat, subcutaneous	<0.01	<0.01	<0.01
Kidney	<0.01	0.02	0.05
Liver	<0.01	0.01	0.03

Table 7.	**Maximum Residues of Difenoconazole, CGA 205375, and 1,2,4-Triazole in Cattle Milk and Tissues by Feeding Level.**		
Matrix	Maximum Residues by Feeding Level (ppm)		
	0.94 ppm	4.24 ppm	14.3 ppm
Muscle, round	<0.01	0.01	0.04
Muscle, tenderloin	<0.01	0.02	0.04
Muscle, diaphragm	<0.01	0.01	0.04

Residues of CGA 205375 were found to have a linear relationship with the dosing levels in fat, liver, and kidney. Residues of CGA 205375 in milk and muscle, and residues of difenoconazole and 1,2,4-T in milk and all tissues were too low to allow determination of the linearity of the dose response. Residues of CGA 205375 and 1,2,4-T appeared to reach a plateau in milk by dosing days 5 and 8, respectively.

Conclusions. Tolerances are currently established for residues of difenoconazole and its metabolite CGA 205375 in livestock commodities at 0.01 ppm for milk; 0.05 ppm for the meat of cattle, goat, hog, horse, and sheep; 0.10 ppm for the fat and meat byproducts (except liver) of cattle, goat, hog, horse, and sheep; and 0.20 ppm for the liver of cattle, goat, hog, horse, and sheep. Based on the calculated dietary burdens and the feeding study data, HED concludes that the subject established tolerances for milk, meat, fat, and meat byproducts (except liver) are adequate to support the proposed uses; however, the tolerance levels for residues of concern in liver of cattle, goat, hog, horse, and sheep should be increased from 0.20 ppm to 0.40 ppm.

Poultry

Syngenta Crop Protection, Inc. previously submitted a poultry feeding study with difenoconazole (MRID 46950224) which was reviewed by HED (PP# 6F7115; D340379, 8/9/07, W. Wassell and M. Sahafeyan). These data are the basis for established tolerances for residues of difenoconazole and its metabolite CGA-205375 in poultry commodities.

Four treatment groups of fifteen laying hens each were dosed with difenoconazole at 0.3, 1, 3, and 10 ppm in the feed for 28 consecutive days. The dosing rates correspond to approximately 2.7x, 9x, 27x, and 91x the theoretical dietary burden.

Composite samples of eggs were collected from each subgroup (three subgroups per treatment group) on days 0 (pre-dose), 1, 3, 6, 9, 13, 16, 20, 23 and 28. Composite samples of tissues (skin plus attached fat, peritoneal fat, liver and breast plus thigh muscle) were collected at sacrifice, 20-24 hours after the treated feed had been removed from the hens and replaced with untreated feed.

Egg and tissue samples were analyzed for residues of difenoconazole and CGA 205375 using an LC/MS/MS method, REM 147.07 (precursor to the current enforcement Method 147.07b), and for residues of 1,2,4-T using an LC/MS/MS method, RAM 455/01. These methods are adequate for data collection based on acceptable method recoveries. The validated LOQ for REM 147.07, determined as the LLMV, was 0.01 ppm for each analyte in eggs and tissues. The validated LOQ for RAM 455/01, determined as the LLMV, was 0.01 ppm in liver and 0.005 ppm in all other matrices. No limits of detection were reported for either method.

The maximum residues of difenoconazole, CGA 205375, and 1,2,4-triazole in eggs and tissues at each dosing level are presented in the Table 8 below.

Table 8. Maximum Residues of Difenoconazole, CGA 205375, and 1,2,4-Triazole in Poultry Egg and Tissues by Feeding Level.

Matrix	Maximum Residues by Feeding Level (ppm)			
	0.3 ppm	1 ppm	3 ppm	10 ppm
Difenoconazole Residues				
Eggs	<0.01	<0.01	<0.01	<0.01
Skin plus attached fat	Not analyzed (N/A)	N/A	<0.01	<0.01
Peritoneal fat	N/A	N/A	<0.01	<0.01
Liver	N/A	N/A	<0.01	<0.01
Muscle	N/A	N/A	<0.01	<0.01
CGA 205375 Residues				
Eggs	<0.01	0.01	0.04	0.17
Skin plus attached fat	N/A	N/A	<0.01	<0.01
Peritoneal fat	N/A	N/A	<0.01	<0.01
Liver	N/A	N/A	<0.01	<0.01
Muscle	N/A	N/A	<0.01	<0.01
1,2,4-Triazole Residues				
Eggs	<0.005	0.010	0.024	0.069
Skin plus attached fat	N/A	<0.005	0.005	0.014
Peritoneal fat	N/A	<0.005	<0.005	<0.005
Liver	N/A	<0.01	<0.01	0.02
Muscle	N/A	<0.005	0.008	0.023

Residues of CGA 205375 and 1,2,4-T were found to have a linear relationship with the dosing levels in eggs. Residues of CGA 205375 and 1,2,4-T in tissues and residues of difenoconazole in eggs and tissues were too low to allow determination of the linearity of the dose response. Residues of CGA 205375 and 1,2,4-T appeared to reach a plateau in eggs by dosing days 13 and 6, respectively.

Conclusions: A tolerance is currently established for residues of difenoconazole and its metabolite CGA 205375 in eggs at 0.10 ppm. Based on the calculated poultry dietary burden and the feeding study data, HED concludes that there is no reasonable expectation of finite residues of concern in poultry tissues and no tolerances are needed for these commodities; however, the tolerance level for residues of concern in eggs should be decreased from 0.10 ppm to 0.02 ppm. The new tolerance level is set at the combined LOQ (0.02 ppm; 0.01 ppm for each analyte) of the current livestock tolerance enforcement method (Method 147.07b) which is lower than that of the former enforcement method.

860.1500 Crop Field Trials

Carrots
DER Reference: 47929804.der.doc

Syngenta Crop Protection, Inc. has submitted crop field trial data for difenoconazole in/on carrots. Eight carrot field trials were conducted in the United States encompassing Zones 3 (FL; 1 trial), 5 (ND; 1 trial), 6 (TX; 1 trial), 10 (CA; 4 trials), and 11 (ID; 1 trial) during the 2008 and 2009 growing seasons. Each trial site consisted of one untreated plot and one treated plot. Each treated plot received four foliar broadcast applications of a 2.08 lb/gal emulsifiable concentrate (EC) formulation of difenoconazole at ~0.115 lb ai/A per application, with a 5- to 8-day retreatment interval, for a total seasonal rate of ~0.460 lb ai/A. Applications were made using ground equipment, in ~16-49 gal/A spray volumes, using either a non-ionic surfactant or crop oil concentrate as an adjuvant with one exception. No adjuvant was added to the first treatment at the ID trial. Carrot root samples were harvested 7 days after the last application (DALA). At one trial site (Fresno, CA), samples were also collected at 0, 3, 7, 10, and 14 DALA to assess residue decline.

The results of the carrot field trials are presented in Table 9. Following four broadcast foliar applications of the EC formulation of difenoconazole plus adjuvant at a total application rate of 0.461-0.472 lb ai/A, residues of difenoconazole ranged from <LOQ (0.01 ppm) to 0.203 ppm in/on carrots at a 7-day PHI. Residues of 1,2,4-T were below the LOQ in/on all samples of carrots harvested 7 days following treatment. Residues of TA and TAA in/on carrot samples harvested at a 7-day PHI ranged 0.012-0.054 ppm and <0.01-0.013 ppm, respectively.

Residue decline data show that residues of difenoconazole were relatively stable from the 0-day to 7-day sampling interval and then declined to <LOQ (0.01 ppm) by the 10-day sampling interval. Residues of 1,2,4-T and TAA were at or near the LOQ (0.01 ppm) in/on all samples from the residue decline trial. Residues of TA in carrots fluctuated over the 14 day sampling period (ranging from 0.024 to 0.054 ppm) with no definite pattern of decline or accumulation.

Table 9. Summary of Residue Data from Carrot Field Trials with Difenoconazole.

Commodity	Total Applic. Rate (lb ai/A)	DALA[1]	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Difenoconazole									
Carrot (root)	0.461 – 0.472	7	16	<0.01	0.203	0.181	0.049	0.062	0.059
1,2,4-Triazole (1,2,4-T)									
Carrot (root)	0.461 – 0.472	7	16	<0.01	<0.01	<0.01	ND	<0.01	NA
Triazolylalanine (TA)									
Carrot (root)	0.461 – 0.472	7	16	0.012	0.054	0.054	0.022	0.027	0.013
Triazolyl acetic acid (TAA)									
Carrot (root)	0.461 – 0.472	7	16	<0.01	0.013	0.012	<0.01	<0.01	0.003

1 DALA = Days after the last application.
2 Mean, median, HAFT, and standard deviations were calculated by the reviewer. The LOQ (0.01 ppm for all analytes) was used for calculations for any results reported as <LOQ.
3 HAFT = Highest Average Field Trial.

Conclusions. The submitted carrot field trial data, conducted with a 2.08 lb/gal EC formulation of difenoconazole and including an adjuvant, adequately reflect the proposed use pattern for carrots. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500 for carrot. The available field trial data will support a tolerance of 0.50 ppm in/on carrot. The tolerance calculations for carrot are presented in Appendix I; the recommended tolerance for residues of difenoconazole in/on carrot (0.50 ppm) is based on a large dataset and calculated using the tolerance spreadsheet at a level well above the maximum residue level found (0.203 ppm) in the supporting magnitude of the residue data.

Syngenta Crop Protection, Inc. is also requesting the use of a 1.05 lb/gal MAI suspension concentrate (SC) formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313) and a 0.73 lb/gal MAI emulsion oil in water (EW) formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317) on carrots with essentially the same use pattern and minimum PHI. However, no carrot field trial data were submitted with either of these formulations. The adequacy of the submitted carrot field trial data conducted with a 2.08 lb/gal EC formulation of difenoconazole to support the proposed uses for the SC and EW formulations is discussed later under separate heading entitled, "Adequacy of the submitted data for the EC formulation to support the proposed uses for the SC and EW formulations."

Chickpea
DER Reference: 47929805.der.doc

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole on chickpeas following four applications of a 2.08 lb/gal emulsifiable concentrate (EC) formulation of difenoconazole. Three chickpea field trials were conducted in the United States encompassing Zones 10 (CA; 1 trial) and 11 (OR; 2 trials) during the 2007 growing season.

Each field trial included one control plot and one treated plot in which the difenoconazole EC formulation was applied to chickpeas. Each plot was treated four times as a foliar broadcast application at a target rate of 0.115 lb ai/A, for a total seasonal nominal rate of 0.46 lb ai/A. Actual total application rates ranged from 0.4613-0.4627 lb ai/A in the chickpea plots. Re-treatment intervals were 14 days. Non-ionic surfactant was added to all spray mixtures. Single control and duplicate treated samples of chickpea seeds were harvested from each plot 14 days after the last application (DALA).

The results of the chickpea field trials are presented in Table 10. Following four broadcast treatment applications of difenoconazole at a total rate of 0.4613-0.4627 lb ai/A, difenoconazole residues were <0.01-0.032 ppm in/on chickpea seed (14 DALA). Samples were also analyzed for 1,2,4-T, TA, and TAA with the following residues: 1,2,4-T and TAA: <0.01 ppm in/on all samples of chickpea seed; TA: 0.116-0.385 ppm in/on chickpea seed.

Table 10. Summary of Residue Data from Chickpea Field Trials with Difenoconazole.

Commodity	Total Applic. Rate (lb ai/A)	DALA[1]	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Difenoconazole									
Chickpea, seed	0.4613-0.4627	14	6	<0.01	0.032	0.031	0.01	0.017	0.011
1,2,4-Triazole (1,2,4-T)									
Chickpea, seed	0.4613-0.4627	14	6	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Triazolylalanine (TA)									
Chickpea, seed	0.4613-0.4627	14	6	0.116	0.385	0.383	0.181	0.228	0.124
Triazolyl acetic acid (TAA)									
Chickpea, seed	0.4613-0.4627	14	6	<0.01	<0.01	<0.01	<0.01	<0.01	NA

1 DALA = Days after the last application.
2 Mean, median, HAFT, and standard deviations were calculated by the reviewer. The LOQ (0.01 ppm for all analytes) was used for calculations for any results reported as <LOQ.
3 HAFT = Highest Average Field Trial.

Conclusions. With the exception of the proposed retreatment interval (7-day RTI), the submitted chickpea field trial data, conducted with a 2.08 lb/gal EC formulation of difenoconazole and including an adjuvant, adequately reflect the proposed use pattern for chickpeas. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500 for chickpeas. The available field trial data will support a tolerance of 0.08 ppm in/on chickpea. The tolerance calculations for chickpeas are presented in Appendix I; the recommended tolerance for residues of difenoconazole in/on chickpeas (0.08 ppm) is based on a small dataset and calculated using the tolerance spreadsheet at a level well above the maximum residue level found (0.032 ppm) in the supporting magnitude of the residue data.

Syngenta Crop Protection, Inc. is also requesting the use of a 1.05 lb/gal MAI suspension concentrate (SC) formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313) and a 0.73 lb/gal MAI emulsion oil in water (EW) formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317) on chickpeas with essentially the same use pattern and minimum PHI. However, no chickpea field trial data were submitted with either of these formulations. The adequacy of the submitted chickpea field trial data conducted with a 2.08 lb/gal EC formulation of difenoconazole to support the proposed uses for the SC and EW formulations is discussed later under separate heading entitled, "Adequacy of the submitted data for the EC formulation to support the proposed uses for the SC and EW formulations."

Soybean
DER Reference: 47929801.de1.doc

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole in/on soybeans following two applications of a 2.08 lb/gal emulsifiable concentrate (EC) formulation of difenoconazole. Twenty-one soybean field trials were conducted in the United States encompassing Zones 2 (NC; 2 trials), 4 (MO and LA; 3 trials), and 5 (MO, WI, ND, NE, IA, and MN; 16 trials) during the 2008 growing season.

Each field trial included one control plot and two treated plots (one for soybean forage and hay and one for soybean seed) in which the difenoconazole EC formulation was applied to soybeans. Each plot was treated twice as a foliar broadcast application at a target rate of 0.11 lb ai/A, for a total seasonal nominal rate of 0.22 lb ai/A. Actual total application rates ranged from 0.2146-0.2293 lb ai/A in the forage/hay plots and 0.2175-0.2244 lb ai/A in the seed plots. Re-treatment intervals ranged from 5 to 8 days. Crop oil concentrate or non-ionic surfactant was added to all spray mixtures. Single control and duplicate treated samples of soybean (forage, hay, and seed) were harvested from each plot on the day of the last application (0 DALA) for forage and hay and 11-17 DALA for seed.

The results of the soybean field trials are presented in Table 11. Following two broadcast treatment applications of difenoconazole at a total rate of 0.2146-0.2293 lb ai/A, difenoconazole residues were 5.2-14.3 ppm in/on soybean forage (0 DALA), 8.64-51.8 ppm in/on soybean hay (0 DALA), and <0.01-0.152 ppm in/on soybean seed (11-17 DALA). Samples were also analyzed for 1,2,4-T, TA, and TAA with the following residues: 1,2,4-T: <0.01 ppm in/on all samples of soybean forage, hay, and seed; TA: <0.01-0.0755 ppm in/on soybean forage, <0.01-0.158 ppm in/on soybean hay, and 0.0295-0.282 ppm in/on soybean seed; and TAA: <0.01-0.013 ppm in/on soybean forage, <0.01-0.0515 ppm in/on soybean hay, and <0.01-0.020 ppm in/on soybean seed.

At two trial sites (NC and IA), samples of soybean forage and hay were taken at 0, 3, 7, and 14 days PHI and samples of soybean seed were taken at 0, 7, 14, 20-21, and 28-33 DALA to assess residue decline. At all trial sites, difenoconazole residues in/on soybean (forage, hay, and straw) declined steadily from 0 DALA to longer post-treatment intervals. Residues of difenoconazole *per se* in/on soybean seeds declined only slightly between 14 DALA (proposed PHI for soybean seeds) and 28-33 DALA.

Table 11. Summary of Residue Data from Soybean Field Trials with Difenoconazole.

Commodity	Total Applic. Rate (lb ai/A)	DALA[1]	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Difenoconazole									
Soybean forage	0.2146-0.2293	0	40	5.24	14.3	13.9	8.91	9.04	2.5
Soybean hay	0.2146-0.2293	0	40	8.64	51.8	43.4	22.8	23.6	10.8
Soybean seed	0.2175-0.2244	11-17	40	<0.01	0.152	0.0869	0.01	0.0215	0.0
1,2,4-Triazole (1,2,4-T)									
Soybean forage	0.2146-0.2293	0	40	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Soybean hay	0.2146-0.2293	0	40	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Soybean seed	0.2175-0.2244	11-17	40	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Triazolylalanine (TA)									
Soybean forage	0.2146-0.2293	0	40	<0.01	0.0755	0.0715	0.0231	0.0257	0.0
Soybean hay	0.2146-0.2293	0	40	<0.01	0.158	0.128	0.0372	0.0443	0.0
Soybean seed	0.2175-0.2244	11-17	40	0.0295	0.282	0.273	0.0855	0.107	0.1
Triazolyl acetic acid (TAA)									
Soybean forage	0.2146-0.2293	0	40	<0.01	0.013	0.0119	0.01	0.0101	0.0
Soybean hay	0.2146-0.2293	0	40	<0.01	0.0515	0.0490	0.0194	0.0230	0.0
Soybean seed	0.2175-0.2244	11-17	40	<0.01	0.020	0.018	0.01	0.011	0.0

1 DALA = Days after the last application.
2 Mean, median, HAFT, and standard deviations were calculated by the reviewer. The LOQ (0.01 ppm for all analytes) was used for calculations for any results reported as <LOQ.
3 HAFT = Highest Average Field Trial.

Conclusions. The submitted soybean seed field trial data, conducted with a 2.08 lb/gal EC formulation of difenoconazole and including an adjuvant, will support a maximum use on soybean of two applications at 0.11 lb ai/A/application for a total seasonal application rate of 0.22 lb ai/A with a 7-day RTI and a 14-day PHI. Labels must be revised to reflect the maximum use rate support by the available data. The petitioner is proposing a feeding restriction on forage and hay. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500 for soybean. The available field trial data will support a tolerance of 0.15 ppm in/on soybean seed. The tolerance calculations for soybean seed are presented in Appendix I; the recommended tolerance for residues of difenoconazole in/on soybean seed (0.15 ppm) is based on a large dataset and calculated using the tolerance spreadsheet at a level equal to the maximum residue level (0.152 ppm) but well below the highest average field trial level found (0.0869 ppm) in the supporting magnitude of the residue data.

Syngenta Crop Protection, Inc. is also requesting the use of a 1.05 lb/gal MAI suspension concentrate (SC) formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313) on soybeans with essentially the same use pattern and minimum PHI. However, no soybean seed field trial data were submitted with a SC formulation. The adequacy of the submitted soybean seed field trial data conducted with a 2.08 lb/gal EC formulation of difenoconazole to support the proposed use for the SC formulation is discussed later under separate heading entitled, "Adequacy of the submitted data for the EC formulation to support the proposed uses for the SC and EW formulations."

Stone Fruit, Group 12
DER Reference: 47929803.de1.doc

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole on stone fruit (Crop Group 12) following four applications of a 2.08 lb/gal emulsifiable concentrate (EC) of difenoconazole. Twenty-one stone fruit field trials were conducted in the United States and Canada during the 2008-2009 growing seasons. Six cherry trials (2 tart cherry; 4 sweet cherry) were conducted in Zones 1 (PA; 1 trial), 5 (MI; 1 trial), 10 (CA; 2 trials), and 11 (WA; 2 trials); nine peach trials were conducted in Zones 1 (NY; 1 trial), 2 (GA and NC; 3 trials), 5 (Ontario, Canada; 1 trial), 6 (TX; 1 trial), and 10 (CA; 3 trials); and six plum trials were conducted in Zones 5 (MI; 1 trial), 10 (CA; 4 trials), and 12 (OR; 1 trial).

Each field trial included one control plot and one treated plot in which the difenoconazole EC formulation was applied to stone fruit. Each plot was treated four times as a foliar broadcast application at a target rate of 0.115 lb ai/A, for a total seasonal nominal rate of 0.46 lb ai/A. Actual total application rates ranged from 0.46-0.47 lb ai/A on the sweet cherry plots, 0.46-0.47 lb ai/A on the tart cherry plots, 0.46-0.49 lb ai/A on the peach plots, and 0.46-0.46 lb ai/A on the plum plots. Re-treatment intervals ranged from 5 to 8 days. Crop oil concentrate, non-ionic surfactant, or miscible oil was added to all spray mixtures. Both dilute and concentrated spray volumes were represented in cherry, peach, and plum field trials. Single control and duplicate treated samples of stone fruit (sweet cherry, tart cherry, peach, or plum) were harvested from each plot on the day of the last application (0 DALA).

The results of the stone fruit field trials are presented in Table 12. Following four broadcast applications of difenoconazole at a total rate of 0.4557-0.4713 lb ai/A, difenoconazole residues were 0.284-0.716 ppm in/on sweet cherry (0 DALA), 0.728-1.01 ppm in/on tart cherry (0 DALA), 0.073-1.02 ppm in/on peach (0 DALA), and 0.070-0.600 ppm in/on plum (0 DALA). Samples were also analyzed for 1,2,4-T, TA, and TAA with the following residues: 1,2,4-T: <0.01 ppm in/on all samples of sweet cherry, tart cherry, peach, and plum; TA: 0.021-0.106 ppm in/on sweet cherry, 0.236-1.42 ppm in/on tart cherry, <0.01-0.825 ppm in/on peach, and 0.019-0.337 ppm in/on plum; and TAA: <0.01 ppm in/on sweet cherry, 0.011-0.096 ppm in/on tart cherry, <0.01-0.055 ppm in/on peach, and <0.01-0.011 ppm in/on plum.

At two trial sites (Fresno and Hughson, CA), samples of sweet cherry or peaches were taken at 0, 1, and 3 DALA to assess residue decline. At both trial sites, difenoconazole residues in/on sweet cherries and peaches declined only slightly at the slightly longer post-treatment intervals.

Table 12. Summary of Residue Data from Stone Fruit Crop Field Trials with Difenoconazole.

Commodity	Total Applic. Rate lb ai/A (kg ai/ha)	DALA [1]	Residue Levels (ppm)[2]						
			N	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Difenoconazole									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	0.284	0.716	0.694	0.475	0.504	0.167
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	0.728	1.01	0.949	0.846	0.858	0.121
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	0.0728	1.02	0.950	0.337	0.421	0.298
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	0.070	0.600	0.543	0.321	0.295	0.168
1,2,4-Triazole (1,2,4-T)									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Triazolylalanine (TA)									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	0.0211	0.106	0.102	0.064	0.063	0.030
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	0.236	1.42	1.31	0.834	0.831	0.568
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	<0.01	0.825	0.760	0.053	0.140	0.232
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	0.0187	0.337	0.297	0.0726	0.117	0.104
Triazolyl acetic acid (TAA)									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	0.0113	0.0955	0.0923	0.0562	0.055	0.044
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	<0.01	0.0545	0.054	0.010	0.017	0.015
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	<0.01	0.0114	0.0112	0.010	0.010	0.000

1 DALA = Days after last application.
2 Mean, median, HAFT, and standard deviations were calculated by the reviewer. The LOQ (0.01 ppm for all analytes) was used for calculations for any results reported as <LOQ.
3 HAFT = Highest Average Field Trial

Conclusions. The submitted stone fruit field trial data, conducted with a 2.08 lb/gal EC formulation of difenoconazole and including an adjuvant, adequately reflect the proposed use pattern for stone fruits. The number and locations of peach and plum field trials are in accordance with OPPTS Guideline 860.1500.

While the number of cherry field trials (6 in total) is in accordance with OPPTS Guideline 860.1500, there was some deviation from the guidelines with regards to the geographical locations represented since trials were conducted for both tart (2 trials) and sweet (4 trials) cherries. [*See 47929803.de1.doc for details.*] However, given that the proposed PHI is 0-days for cherries, residue levels in/on cherries is not likely to be significantly affected by regional influences. Hence, the submitted cherry field trails are deemed adequate to support the proposed use pattern for stone fruits.

The available field trial data will support a tolerance of 2.5 ppm in/on Fruit, stone, group 12. The tolerance calculations for stone fruits are presented in Appendix I; the recommended tolerance for residues of difenoconazole in/on stone fruits (2.5 ppm), which is the tolerance recommended for peach, is based on a large dataset and calculated using the tolerance spreadsheet at a level well above the maximum residue level found (1.02 ppm) in the supporting magnitude of the residue data.

Syngenta Crop Protection, Inc. is also requesting the use of a 1.05 lb/gal MAI suspension concentrate (SC) formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313) and a 0.73 lb/gal MAI emulsion oil in water (EW) formulation with cyprodinil (Inspire Super ™ Fungicide; EPA Reg. No. 100-1317) on stone fruits with essentially the same use pattern and minimum PHI. However, no stone fruit field trial data were submitted with either of these formulations. The adequacy of the submitted stone fruit field trial data conducted with a 2.08 lb/gal EC formulation of difenoconazole to support the proposed uses for the SC and EW formulations is discussed later under separate heading entitled, "Adequacy of the submitted data for the EC formulation to support the proposed uses for the SC and EW formulations."

Strawberry

DER Reference: 47929802.der.doc

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole in/on strawberries. Nine trials were conducted in the United States during the 2007 and 2009 growing seasons, encompassing Zones 1 (NY; 1 trial), 2 (NC; 1 trial), 3 (FL; 1 trial), 5 (MN; 1 trial), 10 (CA; 4 trials), and 12 (WA; 1 trial). One treated plot and one untreated control plot were established at each trial site. The treated plots each received four foliar broadcast applications of a 2.08 lb/gal emulsifiable concentrate (EC) formulation containing difenoconazole, at a nominal application rate of 0.115 lb ai/A. The total application rate was 0.45-0.47 lb ai/A. Applications were made 6-8 days apart using a backpack sprayer and a spray volume of 5.04 to 51.5 gal/A. One trial (Guadalupe, CA) was conducted at ~5 gal/A spray volume to simulate aerial application. NIS (Silwet, Kinetic or other nonionic surfactant) adjuvant was to the spray mixtures at each test site. Strawberry fruit samples were collected 7 days after the third application and immediately following the fourth (last) application (PHI = 0). Samples were also collected at 1, 3 and 5 days after the last application to generate residue decline data.

The results of the strawberry field trials are presented in Table 13. Following four foliar applications of difenoconazole at a total rate of 0.46 lb ai/A, difenoconazole residues in/on strawberries harvested at a PHI of 0 days ranged from 0.0704 ppm to 1.22 ppm. Samples were also analyzed for 1,2,4-T, TA, and TAA with the following residues: 1,2,4-T: <0.01 ppm in/on all samples of strawberry fruit; TA: <0.01-0.083 ppm in/on strawberry fruit; and TAA: <0.01-0.0123 ppm in/on strawberry fruit. Samples were also collected 7 days after the third application. For those samples, difenoconazole residues in/on strawberries harvested at a PHI of

7 days ranged from 0.0908 ppm to 0.590 ppm. Samples were also analyzed for 1,2,4-T, TA, and TAA with the following residues: 1,2,4-T: <0.01 ppm in/on all samples of strawberry fruit; TA: <0.01-0.0875 ppm in/on strawberry fruit; and TAA: <0.01-0.0257 ppm in/on strawberry fruit.

At the Santa Maria, CA test site (Trial No. W30CA078485), additional samples were collected at 1, 3, and 5 days after the last treatment to determine the decline of difenoconazole. Residues of difenoconazole *per se* in/on strawberry (fruit) were relatively stable from the 0-day to 5-day sampling interval.

Table 13. Summary of Residue Data from Strawberry Crop Field Trials with Difenoconazole.

Commodity	Total Application Rate (lb ai/A)	PHI (days)[1]	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
Difenoconazole									
Strawberries	0.35	7	18	0.0908	0.590	0.565	0.225	0.248	0.130
	0.46	0	18	0.0704	1.22	1.21	0.422	0.495	0.320
1,2,4-Triazole (1,2,4-T)									
Strawberries	0.35	7	18	<0.01	<0.01	<0.01	<0.01	<0.01	NA
	0.46	0	18	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Triazolylalanine (TA)									
Strawberries	0.35	7	18	<0.01	0.0875	0.084	0.035	0.038	0.026
	0.46	0	18	<0.01	0.083	0.0760	0.032	0.038	0.025
Triazolyl acetic acid (TAA)									
Strawberries	0.35	7	18	<0.01	0.0257	0.0248	0.01	0.012	0.005
	0.46	0	18	<0.01	0.0123	0.0120	0.01	0.01	0.000

1 Samples were collected at two intervals, seven days after the 3rd application and immediately following the 4th and final application.
2 HAFT = Highest Average Field Trial

Conclusions. The submitted strawberry field trial data, conducted with a 2.08 lb/gal EC formulation of difenoconazole and including an adjuvant, adequately reflect the proposed use pattern for strawberry. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500 for strawberry. The available field trial data will support a tolerance of 2.5 in/on strawberry. The tolerance calculations for strawberry are presented in Appendix I: the recommended tolerance for residues of difenoconazole in/on strawberry (2.50 ppm) is based on a large dataset and calculated using the tolerance spreadsheet at a level well above the maximum residue level found (1.22 ppm) in the supporting magnitude of the residue data.

Syngenta Crop Protection, Inc. is also requesting the use of a 1.05 lb/gal MAI suspension concentrate (SC) formulation with azoxystrobin (Quadris Top™ Fungicide; EPA Reg. No. 100-1313) and a 0.73 lb/gal MAI emulsion oil in water (EW) formulation with cyprodinil (Inspire Super™ Fungicide; EPA Reg. No. 100-1317) on strawberries with essentially the same use pattern and minimum PHI. However, no strawberry field trial data were submitted with either of these formulations. The adequacy of the submitted strawberry field trial data conducted with a 2.08 lb/gal EC formulation of difenoconazole to support the proposed uses for the SC and EW formulations is discussed later under separate heading entitled, "Adequacy of the submitted data for the EC formulation to support the proposed uses for the SC and EW formulations."

Turnip Greens

Residue Chemistry Memo DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian (Petition No. PP#8F7482)

According to HED guidance (Reviewer's Guide and Summary of HED ChemSAC Approvals for Amending Crop Group/Subgroups [40 CFR 180.41] and Commodity Definitions [40 CFR 180.1(h)]" June 14, 2006), turnip greens will be removed from Crop Group 2: Leaves of root and tuber vegetables group [40 CFR 180.41 (2)], and it will become a member of Crop Group 5: Brassica leafy vegetables [40 CFR 180.41 (5)]. It will also be a member of Crop Subgroup 5B: Leafy *Brassica* greens. Forage turnip varieties grown for livestock feed uses only will remain in Crop Group 2: Leaves of root and tuber vegetables group.

No turnip green data were provided in the subject submission. In compliance with a previous HED recommendation (PP# 8F7482; DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian), Syngenta Crop Protection, Inc. is proposing the establishment of a tolerance for residues of difenoconazole in/on turnip greens at 35 ppm.

Conclusions. Available mustard greens data for difenoconazole will be translated to support a tolerance for residues of difenoconazole in/on turnip greens at 35 ppm.

Adequacy of the submitted data for the EC formulation to support the proposed uses for the SC and EW formulations

The petitioner has proposed uses of EC, SC, and EW formulations of difenoconazole on carrots, chickpeas, soybeans (excluding the EW formulation), stone fruits, and strawberries, with essentially the same use patterns and minimum PHIs. The submitted crop field trial data reflect applications of an EC formulation of difenoconazole; no field trial data for the SC or EW formulations were provided in the subject submissions.

Syngenta Crop Protection, Inc. has previously submitted side-by-side field trial data for leaf lettuce, mustard greens, and tomatoes comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 2.08 lb/gal SC formulation (DP# 354013, 3/20/09, B. Cropp-Kohlligian). For each crop, three side-by-side tests were conducted in different regions and samples were harvested at a 0-day PHI. Side-by-side field trial data were also previously submitted for the same crops comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 0.73 lb/gal EW formulation. For each crop, three side-by-side tests were conducted in different regions; samples of leaf lettuce and tomato were harvested at a 0-day PHI and samples of mustard greens were harvested at a 7-day PHI. These previously submitted side-by-side field trial data are summarized in Table 14 below.

When comparing the highest average field trial (HAFT) and mean residue levels from the side-by-side field trial data for the EC and SC formulations, residues of difenoconazole *per se* were found to be higher for the EC formulation than for the SC formulation. Given that all samples were harvested at 0-day PHI, these data are not capable of determining residual differences between the two formulations resulting from longer PHIs.

When comparing the HAFT and mean residue levels from the side-by-side field trial data for the EC and EW formulations, residues of difenoconazole *per se* were found to be higher for the EW formulation than for the EC formulation; HAFT residue levels were found to be 28-54% for the

EW formulation than for the EC formulation. Furthermore, the HED ChemSAC (meeting 01/27/2010) considered these side-by-side field trial data for the EC and EW formulations and noted that the crops are not sufficiently diverse and that before these formulations can be considered equivalent for all crops, a third diverse crop such as grapes should be compared in similar side-by-side trials.

Table 14. Summary of Previously Submitted (DP# 354013) Residue Data from Side-by-side Crop Field Trials Comparing Residues of Difenoconazole from an EC formulation to a SC formulation or EW formulation.

Commodity	Formulation [1]	Total Applic. Rate (lb ai/A)	PHI (days)	Residue Levels (ppm) [2]						
				N	Min.	Max.	HAFT [3]	Median (STMdR)	Mean (STMR)	Std. Dev.
EC vs. SC Formulation										
Leaf lettuce	2.08 lb/gal EC	0.454-0.473	0	6	0.84	5.6	5.6	3.65	3.42	2.07
	2.08 lb/gal SC	0.452-0.465	0	6	0.66	5.5	5.4	2.55	3.01	1.99
Mustard greens	2.08 lb/gal EC	0.459-0.464	0	6	3.50	23.0	20.5	7.90	10.9	7.85
	2.08 lb/gal SC	0.458-0.462	0	6	3.20	18.0	16.0	6.10	8.82	5.81
Tomato	2.08 lb/gal EC	0.461-0.480	0	6	0.08	0.26	0.25	0.12	0.15	0.08
	2.08 lb/gal SC	0.454-0.486	0	6	0.09	0.18	0.17	0.14	0.14	0.04
EC vs. EW Formulation										
Leaf lettuce	2.08 lb/gal EC	0.459-0.474	0	6	2.38	6.68	6.23	4.17	4.40	1.62
	2.82 lb/gal EW	0.454-0.470	0	6	2.57	9.68	9.60	3.99	5.51	3.21
Mustard greens	2.08 lb/gal EC	0.456-0.479	7	6	0.53	3.38	1.96	0.68	1.32	1.17
	2.82 lb/gal EW	0.445-0.477	7	6	0.61	2.96	2.51	1.17	1.45	0.90
Tomato	2.08 lb/gal EC	0.462-0.467	0	6	0.08	0.22	0.20	0.16	0.15	0.06
	2.82 lb/gal EW	0.453-0.467	0	6	0.08	0.31	0.27	0.14	0.17	0.09

1 The EW is a MAI formulation containing 2.09 lb/gal of cyprodinil and 0.73 lb/gal of difenoconazole.
2 The LOQ is 0.01 ppm in/on each commodity.
3 HAFT = Highest Average Field Trial.

Conclusions. Given the limited scope and nature of the previously submitted side-by-side field trial data on leaf lettuce, mustard greens, and tomatoes comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 2.08 lb/gal SC formulation or with that of a 0.73 lb/gal EW formulation discussed above, HED has been reluctant to draw too many conclusions from these data out of context. However, with regards to the crops included in this petition and in consideration of the specific use proposals for the EC and SC formulations of difenoconazole, HED concludes that, collectively, these side-by-side field trial data indicate that residue levels of difenoconazole *per se* in/on the crops included in this petition, with the exception of soybeans, resulting from the proposed multiple late-season foliar applications of a SC formulation should not exceed those resulting from the same use of an EC formulation. Furthermore, having considered the available residue database for difenoconazole which indicates that the recommended tolerances for residues of difenoconazole in/on carrots, chickpeas, stone fruits, and strawberries are based on large datasets, with the exception of chickpeas, and calculated using the tolerance spreadsheet at levels well above the maximum residue level found in the supporting magnitude of the residue data, HED concludes that the recommended tolerances for residues of difenoconazole in/on carrots (0.50 ppm), chickpeas (0.08 ppm), stone fruits (2.5 ppm), and strawberries (2.5 ppm) are likely to cover the proposed uses of the 1.05 lb/gal SC formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries. Hence, HED concludes that the submitted field trial data for the EC formulation may be translated to support the proposed uses of the 1.05 lb/gal SC formulation on carrots, chickpeas, stone fruits, and strawberries provided the petitioner submits a revised Section B/proposed label specifying a minimum RTI of 14-days for chickpeas.

HED concludes that the available leaf lettuce, mustard greens, and tomatoes side-by-side field trial data comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 2.08 lb/gal SC formulation and reflecting a 0-day PHI are not adequate to support the proposed use of the 1.05 lb/gal SC formulation on soybean seeds, which includes a significantly longer PHI (14-days). [Note: There is a proposed restriction against the feeding of soybean hay, forage and silage which is considered to be under grower control.] Furthermore, having considered the available residue database for difenoconazole which indicates that the recommended tolerance for residues of difenoconazole in/on soybean seeds (0.15 ppm) is based on a large dataset and calculated using the tolerance spreadsheet at a level equal to the maximum residue level (0.152 ppm), but well above the highest average field trial (HAFT) level (0.0869 ppm), found in the supporting magnitude of the residue data, additional soybean field trials conducted with the SC formulation at the maximum proposed use rate are required. These data may be field trials conducted with a 25% reduction in number or in the form of limited side-by-side trials conducted to compare residues resulting from the use of an EC formulation with that of the SC formulation. These data are considered confirmatory since, in the meantime, HED concludes that the recommended tolerance for residues of difenoconazole in/on soybean seed (0.15 ppm) is likely to cover the proposed use of the SC formulation of difenoconazole on soybeans provided the petitioner submits a revised Section B/proposed label specifying a maximum seasonal use rate of 0.22 lb ai/A for soybeans.

HED concludes that the available leaf lettuce, mustard greens, and tomatoes side-by-side field trial data comparing residues of difenoconazole *per se* resulting from use of a 2.08 lb/gal EC formulation with that of a 0.73 lb/gal EW formulation, discussed above, indicate that the field trial data for the EC formulation are not adequate to support the proposed uses of the EW formulations addressed in this review. Collectively, these side-by-side field trial data, which represent multiple late-season, foliar applications and 0-7 day PHIs, indicate the potential for significantly higher residue levels of difenoconazole *per se* in/on field crops from the use of the EW formulation when compared to the same use of an EC formulation. The highest average field trial (HAFT) residue levels from the side-by-side field trials were 28-54% higher for the EW formulation than for the EC formulation. However, having considered the available residue database for difenoconazole which indicates that the recommended tolerances for residues of difenoconazole in/on carrots, chickpeas, stone fruits, and strawberries are based on large datasets, with the exception of chickpeas, and calculated using the tolerance spreadsheet at levels well above the maximum residue level found in the supporting magnitude of the residue data, HED concludes that the recommended tolerances for residues of difenoconazole in/on carrots (0.50 ppm), chickpeas (0.08 ppm), stone fruits (2.5 ppm), and strawberries (2.5 ppm) are likely to cover the proposed uses of the 0.73 lb/gal EW formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries. However, given the potential for the 0.73 lb/gal EW formulation to produce higher residues of difenoconazole than the EC formulation and in the absence of sufficient data to fully dispel concerns for that potential in/on carrots, chickpeas, stone fruits, and strawberries, additional data for the 0.73 lb/gal EW formulation of difenoconazole should be submitted as confirmatory evidence. As recommended by ChemSAC (meeting 01/27/2010), additional side-by-side field trials on grapes comparing difenoconazole residues resulting from applications of the EC and EW formulations should provide a more complete and robust dataset to serve as a surrogate for potential residual differences in/on fruits and vegetables at issue. In the meantime, the submitted field trial data representing an EC formulation of difenoconazole are also deemed adequate to support the proposed uses of the EW formulation of difenoconazole on carrots, chickpeas, stone fruits, and strawberries provided the petitioner submits a revised Section B/proposed label specifying a minimum RTI of 14-days for chickpeas.

860.1520 Processed Food and Feed

Plum

DER References: 47929803.de2.doc

Syngenta Crop Protection, Inc. submitted processing studies for difenoconazole on plums. In two crop field trials conducted in CA, a 2.08 lb/gal emulsifiable concentrate (EC) formulation of difenoconazole was applied four times to plums at the label rate (1x) of 0.115 lb ai/A/application for a total nominal application rate of 0.46 lb ai/A (actual application rates of 0.4614-0.4638 lb ai/A) and at an exaggerated rate (3.5x) of 0.403 lb ai/A/application, for a total nominal application rate of 1.6 lb ai/A (actual application rates of 1.622-1.637 lb ai/A). The retreatment intervals (RTIs) were 7-8 days. Plum fruit were harvested at 0 day pre-harvest intervals (PHIs) and processed into prunes by ACDS Research (North Rose, NY) using simulated commercial procedures. Adequate descriptions were provided of the processing procedures, including material balance summaries.

The results of the plum processing study are presented in Table 15. Concentration of difenoconazole and metabolite TA, but not metabolites 1,2,4-T and TAA, following processing at the label rate (1x) and exaggerated rate (3.5x) was observed in prunes. In the 1x trials, residues of difenoconazole were 0.0924-0.644 ppm for plum fruit (RAC) and 0.302-1.07 ppm for prunes; resulting in processing factors of 1.9x and 2.9x. Residues of metabolite TA were 0.0162-0.0432 ppm for plum fruit (RAC) and 0.0488-0.115 ppm for prunes; resulting in processing factors of 2.3x and 3.0x. In the 3.5x trials, residues of difenoconazole were 0.424-1.74 ppm for plum fruit (RAC) and 1.11-4.64 ppm for prunes; resulting in processing factors of 2.7x. Residues of metabolite TA were 0.0424-0.0620 ppm for plum fruit (RAC) and 0.0975-0.144 ppm for prunes; resulting in processing factors of 2.2x and 2.3x. All of the processing factors calculated in this study were less than the maximum theoretical concentration factor of 3.4x for prunes (based on loss of water; OPPTS 860.1520, Table 2).

Soybean
DER References: 47929801.de2.doc

Syngenta Crop Protection, Inc. submitted processing studies for difenoconazole on soybean. In three crop field trials conducted in ND, a 2.08 lb/gal emulsifiable concentrate (EC) formulation of difenoconazole was applied two times to soybean at an exaggerated rate (5x) of 0.55 lb ai/A/application, for a total nominal application rate of 1.1 lb ai/A (actual application rates of 1.09-1.12 lb ai/A). Two trials were conducted to produce processed fraction samples and one trial was conducted to produce aspirated grain fraction (AGF) samples. The retreatment intervals (RTIs) were 7 days. Soybean seed was harvested at 12 to 15 day pre-harvest intervals (PHIs) and processed into AGF, meal, hulls, and refined oil by GLP Technologies (Navasota, TX) using simulated commercial procedures. Adequate descriptions were provided of the processing procedures, including material balance summaries.

The results of the soybean processing study are presented in Table 15. At the Northwood, ND site, in which samples were treated at a total rate 1.09 lb ai/A, residues of difenoconazole in/on soybean seed ranged <0.01-0.0247 ppm; average residues were <LOQ in meal, 0.0538 ppm in hulls, and 0.0169 ppm in refined oil. At the Gardner, ND site, in which samples were treated at a total rate of 1.12 lb ai/A, residues of difenoconazole in/on soybean seed ranged 0.0496-0.107 ppm; average residues were <LOQ in meal, 0.0464 ppm in hulls, and 0.0319 ppm in refined oil. The results of the study indicate that residues of difenoconazole concentrate in hulls (average processing factor of 2.0x) but do not concentrate in meal and refined oil (<1x).

At the Northwood, ND site, residues of TA were 0.113-0.164 ppm in/on soybean seed following treatment at a total rate 1.09 lb ai/A; average residues were 0.148 ppm in meal, 0.0507 ppm in hulls, and <LOQ in refined oil. At the Gardner, ND site, residues of TA were 0.555-0.605 ppm in/on soybean seed following treatment at a total rate 1.12 lb ai/A; average residues were 0.558 ppm in meal, 0.224 ppm in hulls, and <LOQ in refined oil. The results of the study indicate that residues of TA do not concentrate in meal, hulls, and refined oil (≤1x).

At the Northwood, ND site, residues of TAA were below the LOQ (<0.01 ppm) in/on all samples of soybean seed, meal, hulls, and refined oil following treatment at a total rate 1.09 lb ai/A. At the Gardner, ND site, residues of TAA were 0.0194-0.0216 ppm in/on soybean seed following treatment at a total rate 1.12 lb ai/A; average residues were 0.0328 ppm in meal, 0.0139 ppm in hulls, and <LOQ in refined oil. The results of the study indicate that residues of TAA concentrate slightly in meal (average processing factor of 1.3x) but do not concentrate in hulls and refined oil (<1x).

At both sites, residues of metabolite 1,2,4-T were below the LOQ (<0.01 ppm) in/on all samples of soybean seed, meal, hulls, and refined oil. Therefore, no processing factors were calculated.

All of the processing factors calculated in this study were less than the maximum theoretical concentration factors of 11.3x for hulls, 2.2x for meal, and 12.0x for refined oil (based on separation of components; OPPTS 860.1520, Table 3).

Residue data from the soybean AGF study indicate that residues of difenoconazole were 0.310-0.368 ppm in/on soybean seed (RAC) and 190-244 ppm for AGF (resulting in a processing factor of 622x) following treatment at a total rate 1.12 lb ai/A. Residues of metabolite 1,2,4-T were not detected above the LOQ (<0.01 ppm) for soybean seed. Residues of metabolite 1,2,4-T were

0.0210-0.0255 ppm for AGF (resulting in a processing factor of 2.4x). Residues of metabolite TA were 0.590-0.615 ppm for soybean seed and 0.106-0.132 ppm for AGF (resulting in a processing factor of 0.2x) and residues of metabolite TAA were 0.0322-0.0350 ppm for soybean seed and 0.205-0.224 ppm for AGF (resulting in a processing factor of 6.4x).

Table 15. Summary of Processing Factors for Difenoconazole.

RAC	Processed Commodity	Average Processing Factor[1]			
		Difenoconazole	TA	TAA	1,2,4-T
Plum	Prune	2.6x	2.5x	NC	NC
Soybean, seed	Meal	<1x	1.0x	1.3x	NC
	Hulls	2.0x	<1x	<1x	NC
	Refined oil	<1x	NC	NC	NC
Soybean, AGF	--	622x	0.2x	6.4x	2.4x

1 NC = Not calculated; residues were below the LOQ in the RAC and processed commodity.

Conclusions. The submitted plum and soybean processing data for difenoconazole are considered adequate to fulfill data requirements.

The plum processing data indicate that residues of difenoconazole and TA do concentrate in prunes (average processing factors 2.6x and 2.5x, respectively), but residues of 1,2,4-T and TAA do not. For difenoconazole, based on the HAFT for residues in/on plums (0.543 ppm) and the average processing factor (2.6x), expected residues would be 1.4 ppm in prunes. Because this value is lower than the recommended 2.5 ppm tolerance for stone fruits, a separate tolerance is not needed for residues of difenoconazole in prunes.

The soybean processing data indicate that residues of difenoconazole do concentrate in hulls and AGF (average processing factors 2.0x and 622x, respectively), but not in meal and refined oil. Also residues of TAA concentrate slightly in meal (average processing factor 1.3x) and residues of 1,2,4-T and TAA concentrate in AGF (average processing factors 2.4x and 6.4x, respectively). For difenoconazole, based on the HAFT residues in/on soybean seed (0.0869 ppm) and the average processing factor for hulls (2.0x), expected residues would be 0.17 ppm in soybean hulls. Because this value is higher than the recommended 0.15 ppm tolerance for soybean seed, a separate tolerance is needed for residues of difenoconazole in soybean hulls at 0.20 ppm. For difenoconazole, based on the recommended tolerance in/on soybean seed (0.15 ppm) and the average processing factor for AGF (622x), a separate tolerance is needed for residues of difenoconazole in/on AGF at 95 ppm.

860.1650 Submittal of Analytical Reference Standards

Analytical standards for difenoconazole (expiration 11/30/15) and its metabolite CGA-205375 (expiration 8/31/11) are currently available in the EPA National Pesticide Standards Repository (personal communication with Dallas Wright, ACB, email dated 12/7/10).

860.1850 Confined Accumulation in Rotational Crops
Residue Chemistry Memo DP# 344680, 11/5/07, M. Sahafeyan
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

The nature of the residue in rotational crops is not adequately understood because previously conducted studies did not reflect sufficiently high application rates, and/or insufficient characterization/identification of residues was achieved.

The available confined rotational crop data were summarized and reevaluated when the first foliar uses of difenoconazole on crop commodities were proposed (DP# 340379). In two studies, [phenyl-^{14}C]difenoconazole and [triazole-^{14}C]difenoconazole were applied to outdoor plots at a rate of 125 g ai/ha (0.112 lb ai/A; 0.24x the proposed maximum seasonal rate to annual crops). Lettuce was planted at a PBI of 98 days, winter wheat was planted at a 126-day PBI, corn was planted at a 342-day PBI, and sugar beets were planted at a 369-day PBI. No characterization of residues was conducted for phenyl-label crop commodities. In the triazole-label crop commodities that were subjected to characterization/identification procedures (corn grain; wheat grain, straw, and husks; lettuce; and sugar beet tops), 70-82% of the total radioactive residues was identified as a mixture of TA, TAA, and triazole propanoic acid; difenoconazole was not detected. Based on these studies, HED previously concluded that the residue of concern in rotational crops is difenoconazole *per se*.

In a second set of studies, [phenyl-^{14}C]difenoconazole (30.3 µCi/mg) was applied to outdoor plots at a rate of 13.6-14.3 g ai/ha (0.012-0.013 lb ai/A; 0.03x the proposed maximum seasonal rate). Two separate trials were performed. Rotational crops (mustard greens, turnips and wheat) were planted 30-33 days after treatment. The highest residue level was seen in wheat grain (0.007 ppm); therefore, no characterization was conducted. Based on these studies, HED initially concluded that a 30-day plantback interval was appropriate for all crops.

HED subsequently concluded (DP# 340379) that the available confined rotational crop studies were not adequate to support proposed uses on fruiting vegetables, sugar beets, and tuberous and corm vegetables because the studies were conducted at <0.3x the proposed maximum seasonal rate to annual crops of 0.46 lb ai/A, and there were no data delineating the metabolism of the phenyl portion of the molecule in rotational crops. The petitioner was required to submit new confined rotational crop studies reflecting application of [^{14}C]difenoconazole, labeled in the phenyl and triazole rings, at 0.46 lb ai/A.

Syngenta Crop Protection, Inc. responded (letter dated 9/28/07) that adequate data were available from the confined rotational crop, soil metabolism, plant metabolism, and limited rotational crop study results to ascertain the nature of the residue in rotational crops and to establish 30- and 60-day rotational crop intervals.

ChemSAC reviewed the available data and Syngenta's response (meeting of 10/24/07), and concluded that, although additional triazole-ring studies would not be required, a phenyl-ring study was required based on lack of existing data on the phenyl metabolites. The ChemSAC recommended conditional registration of the proposed uses on fruiting vegetables, sugar beets, and tuberous and corm vegetables, with a requirement for a phenyl-label confined rotational crop study to be conducted at 1x the proposed maximum seasonal foliar application rate as a condition of registration. The ChemSAC further concluded that the available data did not support the proposed 30- and 60-day PBIs, and recommended an 8-month PBI until the required phenyl-label CRC study was submitted and reviewed.

Conclusions. The available confined rotational crop data are not adequate to support the proposed uses on carrots, chickpeas, soybeans, and strawberries. The requirement for an additional confined rotational crop study that previously appeared in DP# 344680 is also required to support the proposed uses on carrots, chickpeas, soybeans, and strawberries. A confined rotational crop study reflecting phenyl-ring labeling must be conducted at 1x the proposed maximum seasonal foliar application rate (0.46 lb ai/A). Syngenta Crop Protection, Inc. has submitted a confined rotational crop study (MRID 48203402) which is currently under review in HED (D382946).

860.1900 Field Accumulation in Rotational Crops
Residue Chemistry Memo DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan

Syngenta Crop Protection, Inc. previously submitted an acceptable limited field rotational crop study reflecting application of difenoconazole to a primary crop of tomato at 0.46 lb ai/A. Rotational crops of spinach, radish, and wheat were planted at approximately 30- and 60-day PBIs.

Residues of difenoconazole were <0.01 ppm (<LOQ) in/on all samples of radish root and top, and wheat fall forage, spring forage, hay, grain, and straw from both PBIs (four samples of each commodity at each PBI). Residues of difenoconazole were <0.01 ppm in/on four samples of spinach from the 60-day PBI and two samples of spinach from the 30-day PBI. Quantifiable residues of difenoconazole were observed in/on two samples of spinach from the 30-day PBI, at 0.02 ppm (both samples).

Conclusions. HED previously concluded that provided that difenoconazole is determined to be the only residue of concern in rotational crop commodities, the submitted data are adequate to satisfy data requirements for a limited field rotational crop study. These data will be reevaluated when the outstanding requirement for additional confined rotational crop data is satisfied.

The proposed rotational crop restrictions on the submitted labels are consistent with ChemSAC's recommendation for an 8-month PBI for crops not listed on the label.

860.1550 Proposed Tolerances

Tolerances for plant commodities are established under §180.475(a)(1), and are expressed in terms of difenoconazole *per se*. The tolerance expression proposed by Syngenta is appropriate.

The tolerances proposed by Syngenta Crop Protection, Inc. are listed in Table 16, along with the tolerance levels recommended by HED and corrected commodity definitions.

Provided the petitioner submits a revised Section B/proposed labels specifying a minimum RTI of 14-days for chickpeas and a maximum seasonal use rate of 0.22 lb ai/A for soybeans, adequate field trial data have been submitted to support the proposed uses of the EC formulations of difenoconazole on carrots, chickpeas, soybeans, stone fruits, and strawberries. The submitted data will support the proposed tolerances for stone fruits, group 12 (2.5 ppm) and strawberries (2.5 ppm). The proposed tolerances for carrots (0.45 ppm) and chickpeas (0.05 ppm) are too low; tolerances of 0.50 ppm and 0.08 ppm, respectively, are appropriate. The proposed tolerance for soybean seed (0.20 ppm) is too high; a tolerance of 0.15 ppm is appropriate. The tolerance spreadsheet in the Agency's *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* was utilized for determining appropriate tolerance levels for all raw agricultural commodities, groups, or subgroups listed in Table 16 (see Appendix I).

No turnip green data were provided in the subject submission. In compliance with a previous HED recommendation (PP# 8F7482; DP#s 361054 and 362648, 9/17/09, B. Cropp-Kohlligian), Syngenta Crop Protection, Inc. is proposing the establishment of a tolerance for residues of difenoconazole in/on turnip greens at 35 ppm. Available mustard greens data for difenoconazole will be translated to support a tolerance for residues of difenoconazole in/on turnip greens at 35 ppm. [Note: None of the proposed labels reviewed herein list turnip greens as a separate use site or as a commodity under Brassica leafy vegetables.]

Adequate processing data for plum and soybean seed are available. The plum processing data indicate that residues of difenoconazole do concentrate in prunes; and based on the HAFT for residues in/on plums (0.543 ppm) and the average processing factor (2.6x), expected residues would be 1.4 ppm in prunes. Because this value is lower than the recommended 2.5 ppm tolerance for stone fruits, a separate tolerance is not needed for residues of difenoconazole in prunes. The soybean processing data indicate that residues of difenoconazole do concentrate in hulls and aspirated grain fractions (AGF), but not in meal and refined oil. Based on the HAFT for residues in/on soybean seed (0.0869 ppm) and the average processing factor for hulls (2.0x), expected residues would be 0.17 ppm in soybean hulls. Because this value is higher than the recommended 0.15 ppm tolerance for soybean seed, a separate tolerance is needed for residues of difenoconazole in soybean hulls at 0.20 ppm. Based on the recommended tolerance in/on soybean seed (0.15 ppm) and the average processing factor for AGF (622x), a tolerance is needed for residues of difenoconazole in/on AGF at 95 ppm.

Tolerances are established for the combined residues of difenoconazole and metabolite CGA-250375 in livestock commodities. Acceptable cattle and poultry feeding study data are available. Based on the calculated dietary burdens and the feeding study data, HED concludes that the currently established livestock tolerances for milk, meat, fat, and meat byproducts (except liver) are adequate to support the proposed uses; however, due primarily to the significant change in the beef diet from the proposed use on soybeans and the residues of difenoconazole found in/on soybean AGF, the tolerance levels for residues of concern in liver of cattle, goat, hog, horse, and sheep should be increased from 0.20 ppm to 0.40 ppm. Also, although there was little change in the poultry diet from the new uses, due to the LOQs of the current livestock enforcement method, the tolerance level for residues of concern in egg, should be decreased from 0.10 ppm to 0.02 ppm. Note: The new tolerance level in egg is set at the combined LOQ (0.02 ppm; 0.01 ppm for each analyte) of the current livestock tolerance enforcement method (Method REM 147.07b) which is lower than that of the former enforcement method.

Codex maximum residue levels (MRLs) for residues of difenoconazole *per se* have been established at 0.2 ppm for carrot; 0.02 ppm for soya bean (dry); 0.2 ppm for cherries and plums (including prunes); and 0.5 ppm for nectarines and peaches. Canadian and Mexican MRLs have been established for difenoconazole; however, no MRLs have been established for the requested crops. Codex MRLs for residues of difenoconazole and its metabolite CGA-205375, expressed as difenoconazole have been established at 0.2 ppm for edible offal (mammalian) and 0.01 for eggs. Also, Canadian MRLs have been established for difenoconazole at 0.05 ppm for meat byproducts of cattle, goats, hogs, and sheep and at 0.05 ppm in eggs. Based on the submitted/available magnitude of the residue data, harmonization with established Codex MRLs is not possible for carrots, soya bean (dry), cherries, plums (including prunes), nectarines, peaches, edible offal (mammalian), and eggs because the Codex MRLs are too low. Harmonization with the established Canadian MRLs for eggs and meat byproducts of cattle, goats, hogs, and sheep is not possible due to differences in the tolerance expression. Also based on the available magnitude of the residue data, harmonization with established Canadian MRLs is not possible for meat byproducts of cattle, goats, hops, and sheep because the Canadian MRLs are too low.

The proposed tolerances should be revised to reflect the recommended tolerance levels and correct commodity definitions as specified in Table 16.

Table 16. Tolerance Summary for Difenoconazole.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	*Correct Commodity Definition;* Comments
Carrot	0.45	0.50	
Chickpeas	0.05	0.08	*Chickpea*
Soybean, seed	0.20	0.15	
Soybean, hulls	None	0.20	
Soybean, aspirated grain fraction	95	95	*Aspirated grain fractions*
Fruits, stone, group 12	2.5	2.5	*Fruit, stone, group 12*
Strawberry	2.5	2.5	
Turnip greens	35	35	
Milk	0.08	0.01	No change to the currently established tolerance (0.01 ppm) is warranted.
Liver of cattle, goat, hog, horse, and sheep	None	0.40	Based on the dietary burden, the currently established tolerance should be increased from 0.20 ppm to 0.40 ppm.
Eggs	None	0.02	*Egg* Currently established tolerance should be decreased from 0.10 ppm to 0.02 ppm.

References

DP#s: 172067 and 178394
Subject: PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS#s 9029, 9895.
From: R. Lascola
To: J. Stone/C. Giles-Parker
Dated: 10/26/92
MRIDs: 42090001-42090004, 42090032-42090059, and 42303901

DP#s: 203644 and 203645
Subject: PP#2F4107. Difenoconazole (Dividend) in/on Wheat, and Animal RACs. Amendment of 5/18/94. CBTS# 13771 & 13772.
From: G. Kramer
To: C. Giles-Parker/J. Stone and A. Kocialski
Dated: 6/16/94
MRIDs: 43236501-43236503

DP#: None
Subject: HED Metabolism Committee Meeting of 7/14/94. PP#2F4107 & PP#2E4051. Difenoconazole (Dividend).
From: G. Kramer
To: HED Metabolism Committee
Dated: 7/22/94
MRIDs: None

DP#: 327788
Subject: Triazole-Based Metabolites: Guidance On Residue Chemistry Data Submissions.
From: M. Doherty
To: C. Giles-Parker
Date: 4/25/06
MRIDs: None

DP#: 340379
Subject: PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From: W. Wassell/M. Sahafeyan
To: D. Rosenblatt/S. Brothers
Dated: 8/9/07
MRIDs: 46950215-46950237

DP#: None (ACB memo)
Subject: Review of Proposed Tolerance Enforcement Method for Difenoconazole. ACB Project # B07-26.
From: C. Stafford
To: D. Vogel
Dated: 10/29/07
MRIDs: None

DP#: 344680
Subject: Response to Deficiencies for Petition No. 6F7115, Difenoconazole. Section 3 Registration on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya.
From: M. Sahafeyan
To: T. Kish/J. Whitehurst
Dated: 11/5/07
MRIDs: None

DP#	354013
Subject:	Difenoconazole and Cyprodinil. Registration of a New Multiple Active Ingredient (MAI) End-use Product (Inspire Super™ Fungicide) Formulated as an Emulsion [oil] in Water, Containing Difenoconazole and Cyprodinil, for Use on Pome Fruits. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	L. Jones/T. Kish
Dated:	3/20/09
MRIDs:	47417703-47417708

DP#:	354013
Subject:	Difenoconazole. Crop Field Trial - Mustard greens. DER 47417707.der.doc.
From:	B. Cropp-Kohlligian
Dated:	3/20/09
MRIDs:	47417707

DP#	356135
Subject:	Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	J. Bazuin/T. Kish
Dated:	9/17/09
MRIDs:	47413501 and 47413502

DP#s	361054 and 362648
Subject:	Difenoconazole. Application for Amended Section 3 Registration to Add Uses on Bulb Vegetables, Brassica Leafy Vegetables, Cucurbit Vegetables, Citrus Fruits, Grapes, Pistachios, and Tree Nuts. Submission of Residue Analytical Methods Data in Response to DP#340379. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	9/17/09
MRIDs:	47586101-47586107 and 47648604-47648605

DP#	374898
Subject:	Difenoconazole. The Need for Additional Independent Laboratory Validation (ILV) Information for the Livestock Enforcement Method REM 147.07.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	3/3/10
MRIDs:	None

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.

From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

DP#	375194
Subject:	Difenoconazole. Submission of Storage Stability Data in Livestock Commodities in Response to DP# 340379. Submission of a Report of a New Cattle Feeding Study. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	6/17/10
MRIDs:	47957201-47957203

Attachments:
International Residue Limit Status sheet
Appendix I - Tolerance Assessment Calculations

Template Version September 2005

International Residue Limits

Difenoconazole (128847; 01-13-2011)

Summary of US and International Tolerances and Maximum Residue Limits			
Residue Definition:			
US	Canada	Mexico[2]	Codex[3]
40 CFR 180. 475: Plant: difenoconazole, 1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole. Livestock: difenoconazole, 1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole, and its metabolite, CGA-205375, 1-[2-chloro-4-(4-chloro-phenoxy)phenyl]-2-[1,2,4]triazol-1-yl-ethanol.	1-[2-[4-(4-chlorophenoxy)-2-chlorophenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1 H-1,2,4-triazole.		Plant commodities: difenoconazole Animal commodities: sum of difenoconazole and 1-[2-chloro-4-(4-chloro-phenoxy)-phenyl]-2-(1,2,4-triazol)-1-yl-ethano), expressed as difenoconazole. The residue is fat soluble.

Commodity[1]	*Tolerance (ppm) /Maximum Residue Limit (mg/kg)*			
	US	Canada	Mexico[2]	Codex
Carrot	0.50			0.2
Chickpea	0.08			
Grain, aspirated grain fractions	95			
Soybean, hulls	0.20			
Soybean, seed	0.15			0.02 (*) Soya bean (dry)
Stone fruits	2.5			0.2 Cherries, Plums (including prunes); 0.5 Nectarine, Peach
Strawberry	2.5			
Turnip greens	35			
Cattle, liver	0.40	0.05 Meat byproducts of cattle		0.2 Edible offal (mammalian)
Goat, liver	0.40	0.05 Meat byproducts of goats		0.2 Edible offal (mammalian)
Hog, liver	0.40	0.05 Meat byproducts of hogs		0.2 Edible offal (mammalian)
Horse, liver	0.40			0.2 Edible offal (mammalian)
Sheep, liver	0.40	0.05 Meat byproducts of sheep		0.2 Edible offal (mammalian)
Eggs	0.02	0.05		0.01 (*)
Completed: M. Negussie; 01/19/2011				

[1] Includes only commodities of interest for this action. Tolerance values should be the HED recommendations and not those proposed by the applicant.

[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.

[3] * = absent at the limit of quantitation; Po = postharvest treatment, such as treatment of stored grains. PoP = processed postharvest treated commodity, such as processing of treated stored wheat. (fat) = to be measured on the fat portion of the sample. MRLs indicated as proposed have not been finalized by the CCPR and the CAC.

Appendix I. Tolerance Assessment Calculations.

For each of the crops listed below, the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* (SOP), along with the tolerance spreadsheet (January 2008 version), was used for calculating recommended tolerances. As specified in the SOP, the minimum of the 95% upper confidence limit (UCL) on the 95th percentile and the point estimate of the 99th percentile was selected as the tolerance value in cases when the dataset was large (greater than 15 samples) and reasonably lognormal. For datasets that were small (≤15 samples) and reasonably lognormal, the upper bound estimate of the 95th percentile based on the median residue value was compared to the minimum of the 95% UCL on the 95th percentile and the point estimate of the 99th percentile, and the minimum value was selected as the tolerance value. For datasets that were not lognormal, the upper bound on the 89th percentile was selected as the tolerance value (distribution-free method). The rounding procedures specified in the SOP were also used.

The LOQ for difenoconazole residues in all crop commodities was 0.01 ppm.

Carrot

The dataset used to establish a tolerance for difenoconazole in/on carrot consisted of field trial data representing a maximum seasonal application rate of 0.46 lb ai/A (four applications at 0.115 lb ai/A/application) with a 7-day RTI and a 7-day PHI. The field trial application rates and PHIs are within 25% of the maximum proposed application rates and minimum proposed PHI, respectively. The residue values that were entered into the tolerance spreadsheet are provided in Table I-1.

Only one of the sixteen field trial sample results for difenoconazole in/on carrot was below the LOQ and that sample result was impute into the tolerance spreadsheet at ½LOQ. The dataset was large (16 samples). Visual inspection of the lognormal probability plot (Figure I-1) and the results from the approximate Shapiro-Francia test statistic (Figure I-2) indicated that the carrot dataset was reasonably lognormal.

Using the tolerance spreadsheet, the recommended tolerance is 0.50 ppm in/on carrot.

Table I-1. Residue data used to calculate tolerance for difenoconazole in/on carrot.	
Regulator:	EPA
Chemical:	Difenoconazole
Crop:	Carrot
PHI:	7 days
RTI:	7 days
App. Rate:	0.46 lb ai/A/season (4 applications at 0.115 lb ai/A/application)
Submitter:	Syngenta Crop Protection, Inc.
MRID Citation:	MRID 47929804
	Residues of Difenoconazole (ppm)
	0.005[1]
	0.019
	0.138
	0.050
	0.010
	0.010[2]
	0.084
	0.082
	0.015
	0.021
	0.158
	0.203
	0.054
	0.059
	0.037
	0.048

1 Reported as 0.003184 ppm, below the LOQ (0.01 ppm); estimated at ½LOQ.
2 Reported as 0.00988 ppm, rounded to 0.010 ppm by reviewer.

Figure I-1. Lognormal probability plot of difenoconazole field trial data for carrot.

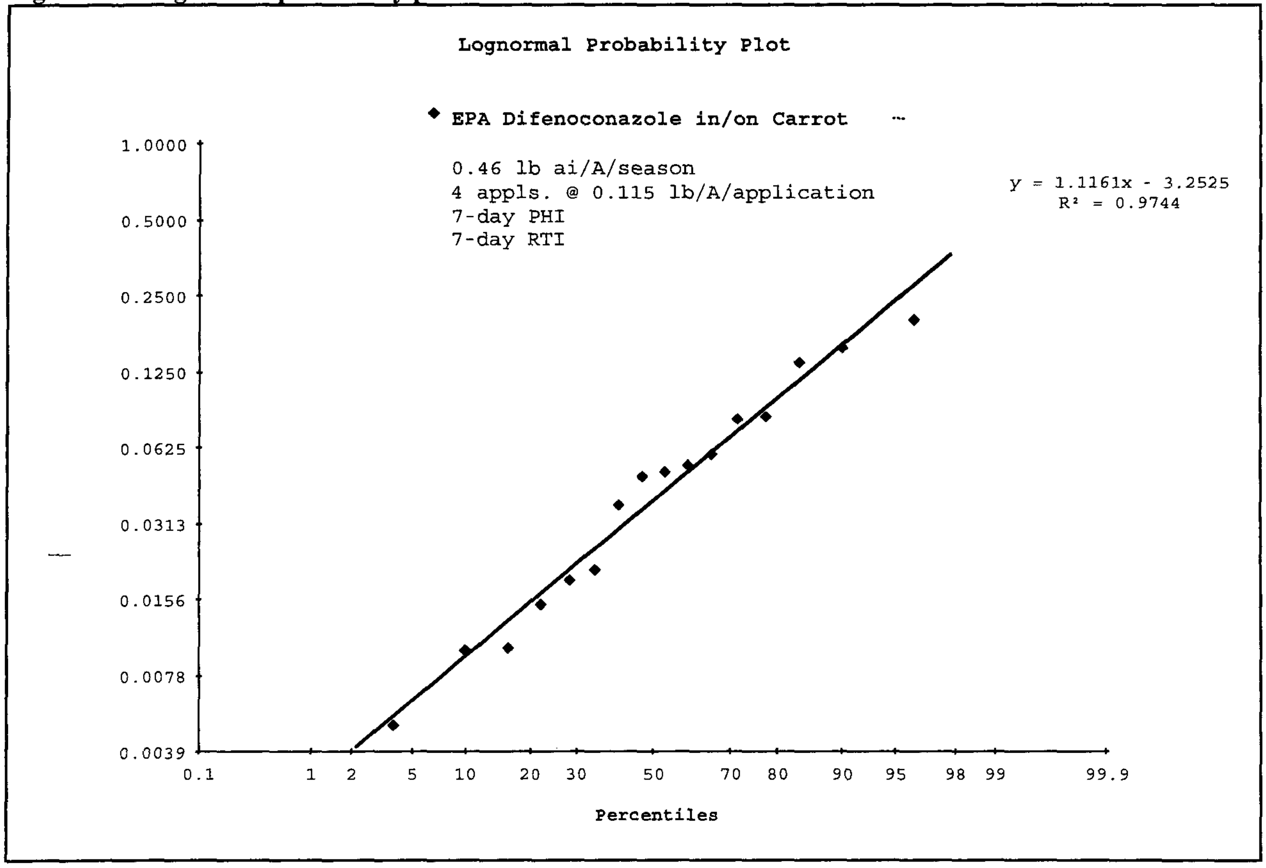


Figure I-2. Tolerance spreadsheet summary of difenoconazole field trial data for carrot.

Regulator: EPA
Chemical: Difenoconazole
Crop: Carrot
PHI: 7 Days
App. Rate: 0.46 lb ai/A (4 appls. @ 0.115 lb ai/A/appl)
Submitter: Syngenta

n: 16
min: 0.01
max: 0.20
median: 0.05
average: 0.06

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.20 (0.25)	0.20 (0.30)	0.25 (--)
95/99 Rule	0.25 **(0.60)**	**0.50** (1.7)	1.1 (--)
EU Method II Distribution-Free	0.20		
Mean+3SD	**0.25**		
UCLMedian95th	**0.30**		
Approximate Shapiro-Francia Normality Test	0.9744 p-value > 0.05 : Do not reject lognormality assumption		

Chickpea

The dataset used to establish a tolerance for difenoconazole in/on chickpea consisted of field trial data representing a maximum seasonal application rate of 0.46 lb ai/A (four applications at 0.115 lb ai/A/application) with a 14-day RTI and a 14-day PHI. The field trial application rates and PHIs are within 25% of the maximum proposed application rate and minimum proposed PHI, respectively. The residue values that were entered into the tolerance spreadsheet are provided in Table I-2.

Because 3 of 6 field trial sample results for difenoconazole in/on chickpea were below the LOQ, maximum likelihood estimation (MLE) procedures were needed to impute censored values. The dataset was small (6 samples). Visual inspection of the lognormal probability plot (Figure I-3) and the results from the approximate Shapiro-Francia test statistic (Figure I-4) indicated that the carrot dataset was reasonably lognormal.

Using the tolerance spreadsheet, the recommended tolerance is 0.08 ppm in/on chickpea.

Table I-2. Residue data used to calculate tolerance for difenoconazole in/on chickpea.	
Regulator:	EPA
Chemical:	Difenoconazole
Crop:	Chickpea
PHI:	14 days
RTI:	14 days
App. Rate:	0.46 lb ai/A/season (4 applications at 0.115 lb ai/A/application)
Submitter:	Syngenta Crop Protection, Inc.
MRID Citation:	MRID 47929805
	Residues of Difenoconazole (ppm)
	0.032
	0.030
	0.010[1]
	0.005[2]
	0.007[2]
	0.008[2]

1 Reported as 0.0096 ppm, rounded to 0.010 ppm by reviewer.
2 Calculated using MLE spreadsheet from a value below the LOQ.

Figure I-3. Lognormal probability plot of difenoconazole field trial data for chickpea.

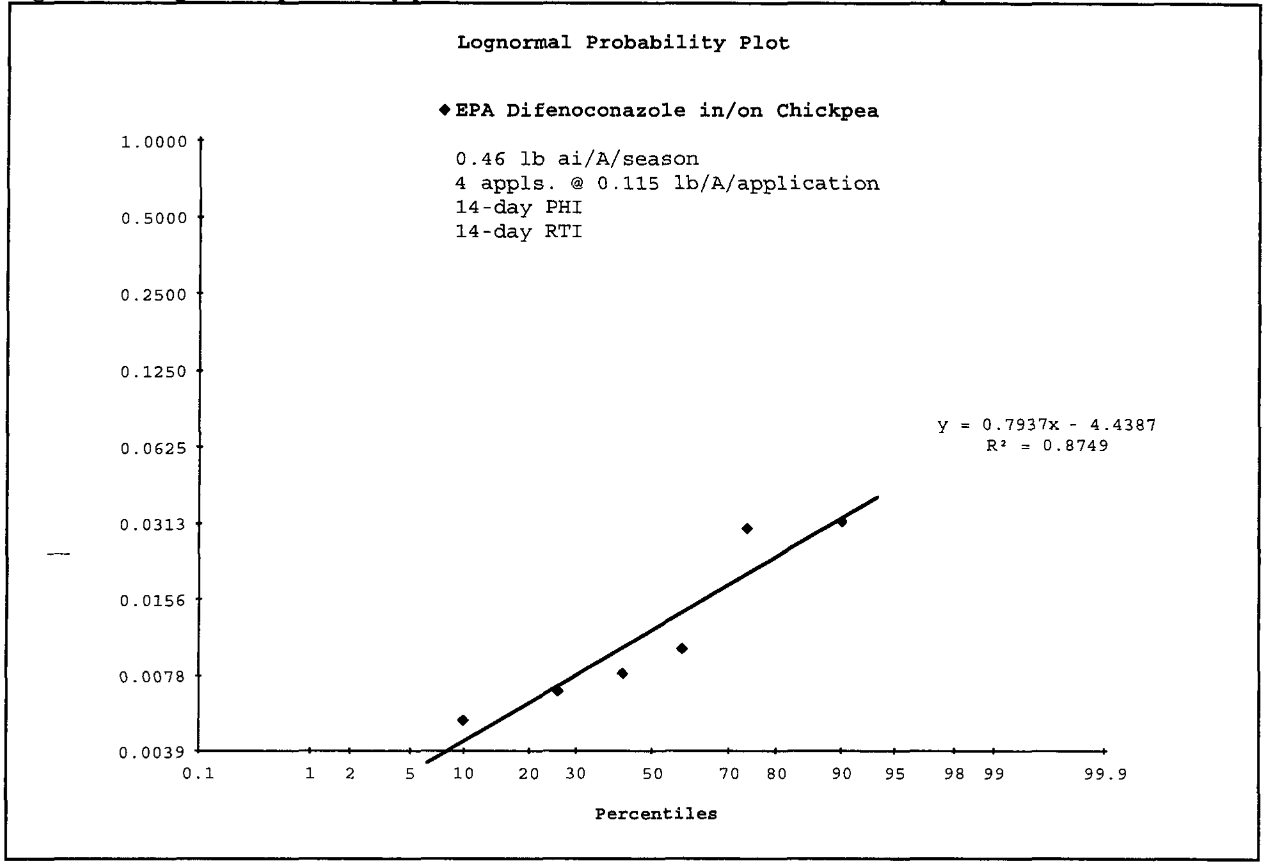


Figure I-4. Tolerance spreadsheet summary of difenoconazole field trial data for chickpea.

	Regulator: EPA **Chemical:** Difenoconazole **Crop:** Chickpea **PHI:** 14 Days **App. Rate:** 0.46 lb ai/A (4 appls at 0.115 lb ai/A/appl) **Submitter:** Syngenta **n:** 6 **min:** 0.01 **max:** 0.03 **median:** 0.01 **average:** 0.02		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.04 (0.07)	0.05 (0.08)	0.06 (--)
95/99 Rule	0.05 (0.25)	0.08 (0.70)	0.15 (--)
EU Method II Distribution-Free		0.07	
Mean+3SD		0.06	
UCLMedian95th		0.08	
Approximate Shapiro-Francia Normality Test	0.8749 p-value > 0.05 : Do not reject lognormality assumption		

Soybean seed

The dataset used to establish a tolerance for difenoconazole in/on soybean seed consisted of field trial data representing a maximum seasonal application rate of 0.22 lb ai/A (two applications at 0.11 lb ai/A/application) with a 7-day RTI and a 14-day PHI. The field trial maximum seasonal application rates (0.22 lb ai/A) are not within 25% of the maximum proposed seasonal application rate (0.46 lb ai/A); but the field trial single application rates (two applications at 0.11 lb ai/A/application) and PHIs are within 25% of the maximum proposed single application rate and minimum proposed PHI, respectively. The residue values that were entered into the tolerance spreadsheet are provided in Table I-3.

Because 23 of 40 (approximately 58%) field trial sample results for difenoconazole in/on soybean seed were below the LOQ, maximum likelihood estimation (MLE) procedures were needed to impute censored values. The dataset was large (40 samples). Visual inspection of the lognormal probability plot (Figure I-5) and the results from the approximate Shapiro-Francia test statistic (Figure I-6) indicated that the soybean seed dataset was not reasonably lognormal.

Using the tolerance spreadsheet, the recommended tolerance is 0.15 ppm for soybean seed.

Table I-3. Residue data used to calculate tolerance for difenoconazole in/on soybean seed.

Regulator:	EPA
Chemical:	Difenoconazole
Crop:	Soybean seed
PHI:	14 days
RTI:	7 days
App. Rate:	0.22 lb ai/A/season (2 applications at 0.11 lb ai/A/application)
Submitter:	Syngenta Crop Protection, Inc.
MRID Citation:	MRID 47929801
	Residues of Difenoconazole (ppm; rounded)
	0.003[1]
	0.004[1]
	0.004[1]
	0.005[1]
	0.005[1]
	0.014
	0.012
	0.019
	0.042
	0.038
	0.012
	0.013
	0.006[1]
	0.006[1]
	0.006[1]
	0.007[1]
	0.026

Table I-3.	**Residue data used to calculate tolerance for difenoconazole in/on soybean seed.**
Regulator:	EPA
Chemical:	Difenoconazole
Crop:	Soybean seed
PHI:	14 days
RTI:	7 days
App. Rate:	0.22 lb ai/A/season (2 applications at 0.11 lb ai/A/application)
Submitter:	Syngenta Crop Protection, Inc.
MRID Citation:	MRID 47929801
	Residues of Difenoconazole (ppm; rounded)
	0.015
	0.007[1]
	0.007[1]
	0.007[1]
	0.008[1]
	0.008[1]
	0.008[1]
	0.008[1]
	0.009[1]
	0.019
	0.018
	0.022
	0.152
	0.067
	0.092
	0.009[1]
	0.009[1]
	0.009[1]
	0.009[1]
	0.044
	0.023
	0.010[1]
	0.010[1]

1 Calculated using MLE spreadsheet from a value below the LOQ.

Figure I-5. Lognormal probability plot of difenoconazole field trial data for soybean seed.

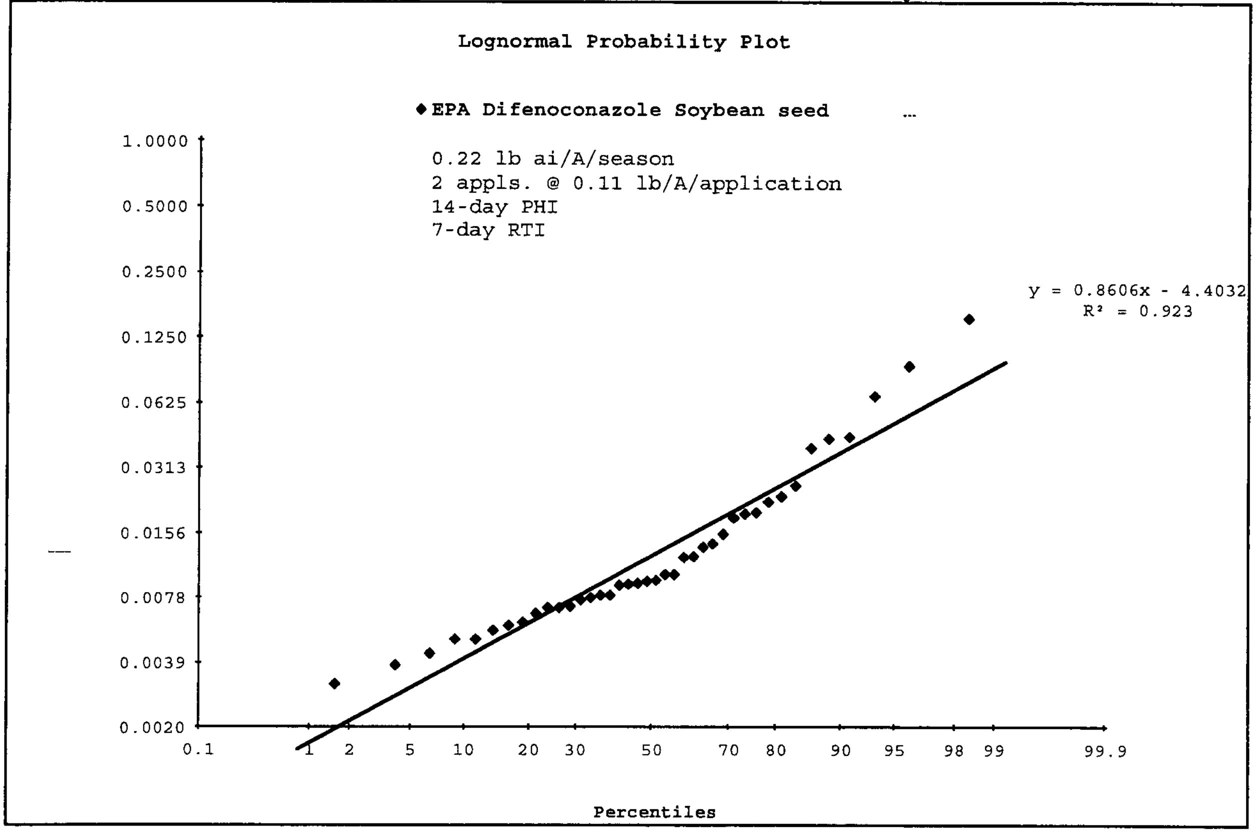


Figure I-6. Tolerance spreadsheet summary of difenoconazole field trial data for soybean seed.

	Regulator: EPA **Chemical:** Difenoconazole **Crop:** Soybean seed **PHI:** 14 Days **App. Rate:** 0.22 lb ai/A (2 appls at 0.11 lb ai/A/appl) **Submitter:** Syngenta **n:** 40 **min:** 0.00 **max:** 0.15 **median:** 0.01 **average:** 0.02		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.07 (0.08)	0.09 (0.15)	0.15 (--)
95/99 Rule	0.06 (0.08)	0.10 (0.20)	0.20 (--)
EU Method II Distribution-Free	0.04		
Mean+3SD	0.15		
UCLMedian95th	0.05		
Approximate Shapiro-Francia Normality Test	0.9230 0.05 >= p-value > 0.01 : Reject lognormality assumption		

Stone fruit, group 12

The dataset used to establish a tolerance for difenoconazole in/on stone fruit consisted of field trial data for cherry, peach, and plum (the representative crops of group 12), representing a maximum seasonal application rate of 0.46 lb ai/A (four applications at 0.115 lb ai/A/application) with a 7-day RTI and a 0-day PHI. The field trial application rates and PHIs are within 25% of the maximum proposed application rates and minimum proposed PHIs, respectively. The residue values that were entered into the tolerance spreadsheet are provided in Table I-4.

All field trial sample results for stone fruit were above the LOQ. The cherry and plum datasets were small (12 samples for sweet/tart cherry and 12 samples for plum), and the peach dataset was large (18 samples). Visual inspection of the lognormal probability plots (Figure I-7, Figure I-9, and Figure I-11) and the results from the approximate Shapiro-Francia test statistics (Figure I-8, Figure I-10, and Figure I-12) indicated that the datasets were reasonably lognormal.

Using the tolerance spreadsheet, the recommended tolerances are 1.5 ppm for cherry, 2.5 ppm for peach, and 1.3 ppm for plum. Because the minimum and maximum recommended tolerances differ by less than 5x, a crop group tolerance is appropriate for stone fruit. The recommended value is 2.5 ppm, the maximum of the recommended individual tolerances.

Table I-4.	**Residue data used to calculate tolerance for difenoconazole on stone fruit.**		
Regulator:	EPA	EPA	EPA
Chemical:	Difenoconazole	Difenoconazole	Difenoconazole
Crop:	Cherry	Peach	Plum
PHI:	0 days		
RTI:	7 days		
App. Rate:	0.46 lb ai/A/season (4 applications at 0.115 lb ai/A/application)		
Submitter:	Syngenta Crop Protection, Inc.		
MRID Citation:	MRID 47929803		
Residues of Difenoconazole (ppm)			
	1.01	0.251	0.358
	0.888	0.319	0.253
	0.804	0.354	0.486
	0.728	0.314	0.600
	0.664	0.880	0.127
	0.494	1.020	0.070
	0.300	0.672	0.082[1]
	0.284	0.872	0.130
	0.716	0.135	0.316
	0.672	0.130	0.326
	0.456	0.652	0.372
	0.448	0.414	0.426
		0.538	
		0.542	
		0.073[1]	
		0.082	
		0.129	
		0.195	

1 Results rounded by reviewer.

Figure I-7. Lognormal probability plot of difenoconazole field trial data for cherry.

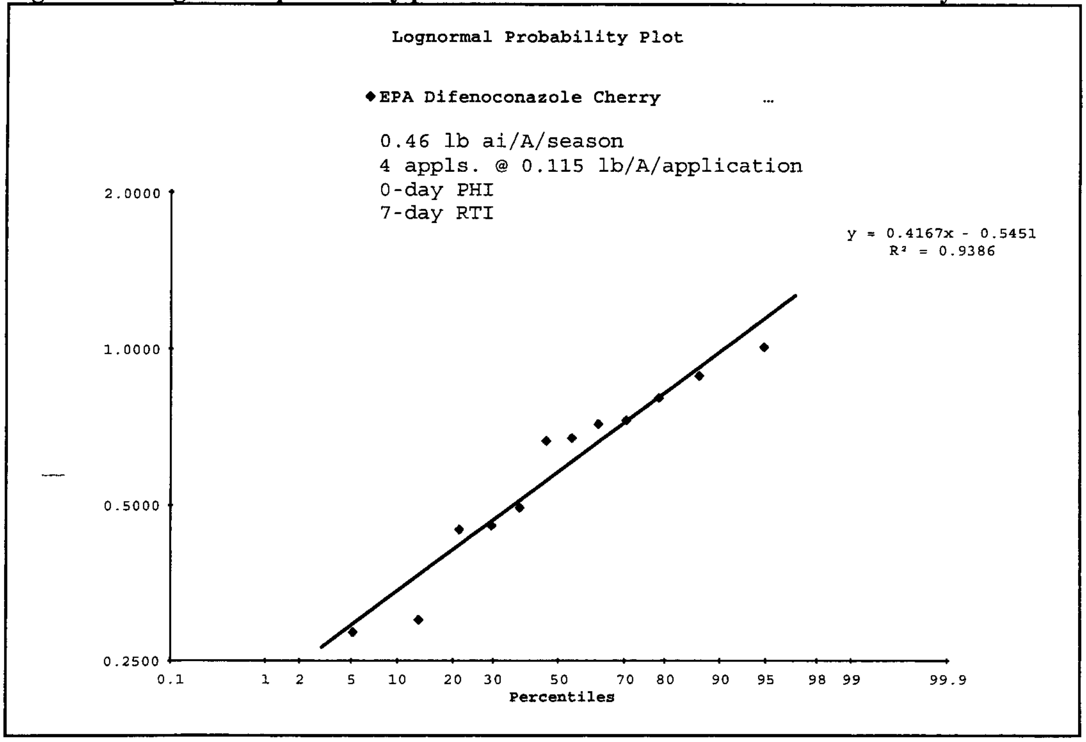


Figure I-8. Tolerance spreadsheet summary of difenoconazole field trial data for cherry.

	Regulator: EPA Chemical: Difenoconazole Crop: Cherry PHI: 0 Days App. Rate: 0.46 lb ai/A (4ppl at 0.115 lb ai/A/appl) Submitter: Syngenta n: 12 min: 0.28 max: 1.01 median: 0.67 average: 0.62		
	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	1.0 (1.3)	1.2 (1.5)	1.4 (--)
95/99 Rule	1.2 (1.8)	1.5 (3.0)	2.5 (--)
EU Method II Distribution-Free	1.6		
Mean+3SD	1.4		
UCLMedian95th	4.5		
Approximate Shapiro-Francia Normality Test	0.9386 p-value > 0.05 : Do not reject lognormality assumption		

Figure I-9. Lognormal probability plot of difenoconazole field trial data for peach.

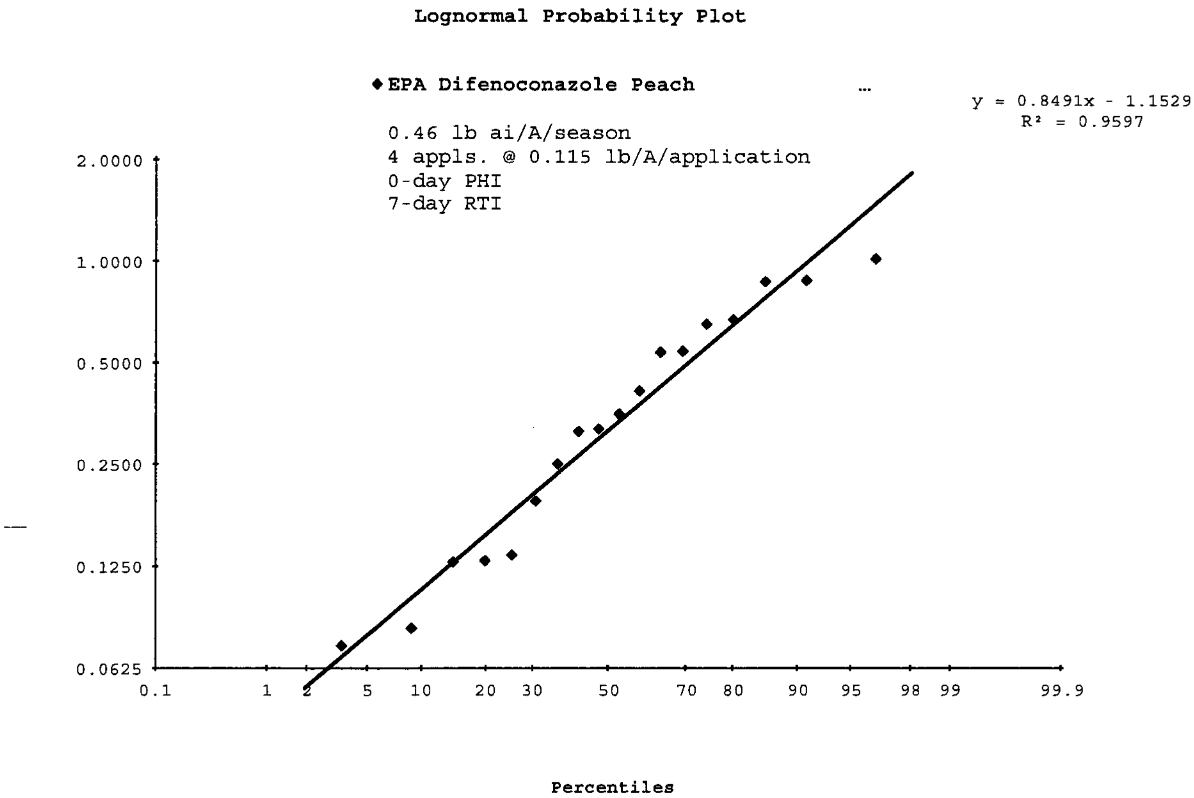


Figure I-10. Tolerance spreadsheet summary of difenoconazole field trial data for peach.

	Regulator: EPA		
	Chemical: Difenoconazole		
	Crop: Peach		
	PHI: 0 Days		
	App. Rate: 0.46 lb ai/A (4ppls at 0.115 lb ai/A/appl)		
	Submitter: Syngenta		
	n: 18		
	min: 0.07		
	max: 1.02		
	median: 0.34		
	average: 0.42		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	1.0 (1.2)	1.2 (1.5)	1.4 (--)
95/99 Rule	1.3 **(2.5)**	**2.5** (6.0)	4.5 (--)
EU Method II Distribution-Free	1.4		
Mean+3SD	**1.4**		
UCLMedian95th	**1.9**		
Approximate Shapiro-Francia Normality Test	0.9597 p-value > 0.05 : Do not reject lognormality assumption		

Figure I-11. Lognormal probability plot of difenoconazole field trial data for plum.

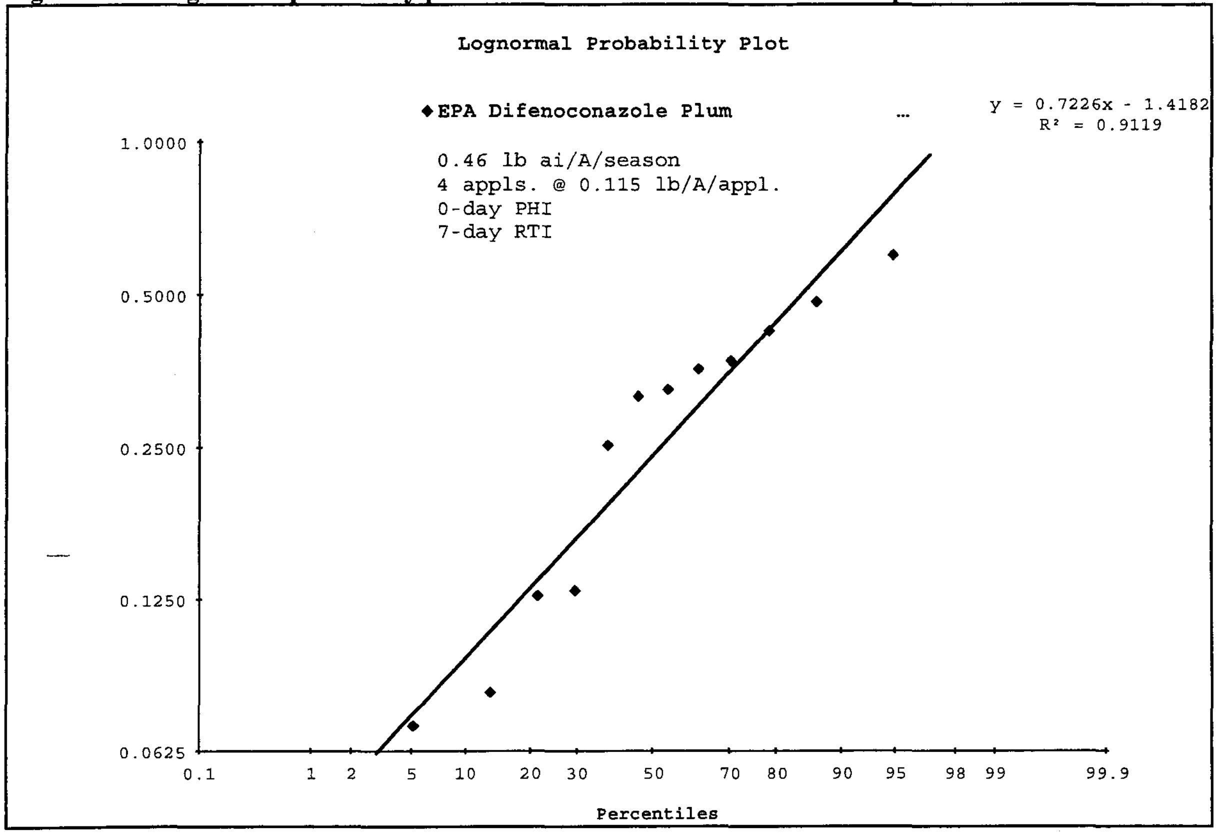


Figure I-12. Tolerance spreadsheet summary of difenoconazole field trial data for plum.

	Regulator: EPA **Chemical:** Difenoconazole **Crop:** Plum **PHI:** 0 Days **App. Rate:** 0.46 lb ai/A (4ppls at 0.115 lb ai/A/appl) **Submitter:** Syngenta **n:** 12 **min:** 0.07 **max:** 0.60 **median:** 0.32 **average:** 0.30		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.60 (0.80)	0.70 (1.0)	0.90 (--)
95/99 Rule	0.80 **(1.8)**	**1.3** (4.0)	2.5 (--)
EU Method II Distribution-Free	0.90		
Mean+3SD	**0.90**		
UCLMedian95th	**2.0**		
Approximate Shapiro-Francia Normality Test	0.9119 p-value > 0.05 : Do not reject lognormality assumption		

Strawberry

The dataset used to establish a tolerance for difenoconazole on strawberry consisted of field trial data representing a maximum seasonal application rate of 0.46 lb ai/A (four applications at 0.115 lb ai/A/application) with a 7-day RTI and a 0-day PHI. The field trial application rates and PHIs are within 25% of the maximum proposed application rate and minimum proposed PHI, respectively. The residue values that were entered into the tolerance spreadsheet are provided in Table I-5.

All field trial sample results for difenoconazole in/on strawberry were above the LOQ. The dataset was large (18 samples). Visual inspection of the lognormal probability plot (Figure I-13) and the results from the approximate Shapiro-Francia test statistic (Figure I-14) indicated that the strawberry dataset was reasonably lognormal.

Using the tolerance spreadsheet, the recommended tolerance is 2.5 ppm in/on strawberry.

Table I-5. Residue data used to calculate tolerance for difenoconazole in/on strawberry.	
Regulator:	EPA
Chemical:	Difenoconazole
Crop:	Strawberry
PHI:	0 days
RTI:	7 days
App. Rate:	0.46 lb ai/A/season (4 applications at 0.115 lb ai/A/application)
Submitter:	Syngenta Crop Protection, Inc.
MRID Citation:	MRID 47929802
	Residues of Difenoconazole (ppm)[1]
	0.638
	0.658
	0.378
	0.432
	0.192
	0.193
	0.485
	0.362
	0.412
	0.554
	0.718
	0.582
	1.200
	1.220
	0.074[1]
	0.070[1]
	0.352
	0.392

1 Results rounded by reviewer.

Figure I-13. Lognormal probability plot of difenoconazole field trial data for strawberry.

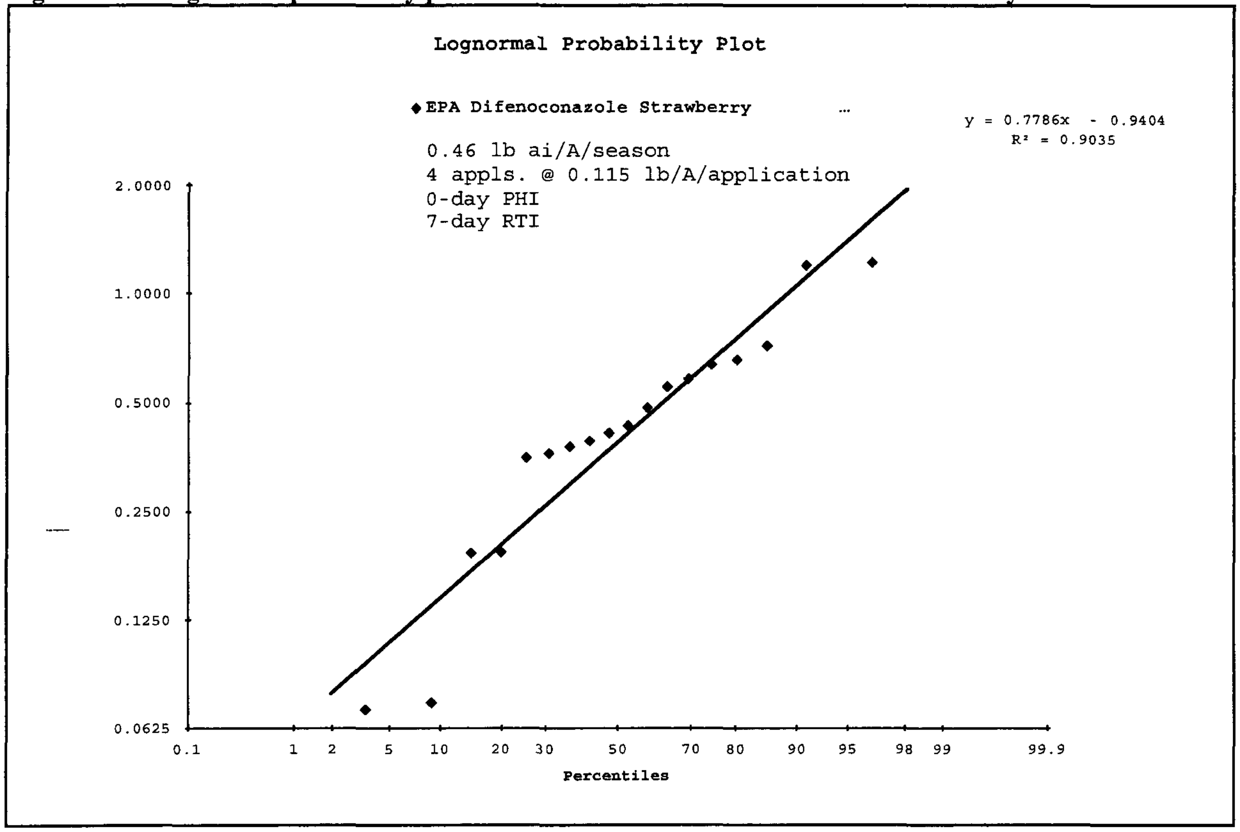


Figure I-14. Tolerance spreadsheet summary of difenoconazole field trial data for strawberry.

	Regulator: EPA		
	Chemical: Difenoconazole		
	Crop: Strawberry		
	PHI: 0 Days		
	App. Rate: 0.46 lb ai/A (4 appls. @ 0.115 lb ai/A/appl.		
	Submitter: Syngenta		
	n: 18		
	min: 0.07		
	max: 1.22		
	median: 0.42		
	average: 0.50		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	1.1 (1.3)	1.3 (1.6)	1.5 (--)
95/99 Rule	1.5 (3.0)	2.5 (6.0)	4.5 (--)
EU Method II Distribution-Free	1.3		
Mean+3SD	1.5		
UCLMedian95th	2.5		
Approximate Shapiro-Francia Normality Test	0.9035 p-value > 0.05 : Do not reject lognormality assumption		

Primary Evaluator: Bonnie Cropp-Kohlligian, Environmental Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)

Bonnie Cropp-Kohlligian

Approved by: Susan V. Hummel, Chemist/Senior Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)

Susan V. Hummel

This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted (1/06/2011). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47929801. Willard, T.; Mayer, T. (2009) Difenoconazole - Magnitude of the Residues in or on Soybean: Final Report. Project Number: T002400-07, ML08-1488-SYN. Unpublished study prepared by Syngenta Crop Protection, Inc. 597 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole in/on soybeans following two applications of an emulsifiable concentrate (EC) formulation containing 2.08 lb ai/gal (Difenoconazole 250 EC). Twenty-one soybean field trials were conducted in the United States encompassing Zones 2 (NC; 2 trials), 4 (MO and LA; 3 trials), and 5 (MO, WI, ND, NE, IA, and MN; 16 trials) during the 2008 growing season. One trial (Gardner, ND) was only conducted at an exaggerated rate to evaluate processing; results are recorded in a separate DER.

Each field trial included one control plot and two treated plots (one for soybean forage and hay and one for soybean seed) in which the difenoconazole EC formulation was applied to soybeans. Each plot was treated twice as a foliar broadcast application at a target rate of 0.11 lb ai/A, for a total seasonal nominal rate of 0.22 lb ai/A. Actual total application rates ranged from 0.2146-0.2293 lb ai/A in the forage/hay plots and 0.2175-0.2244 lb ai/A in the seed plots. Re-treatment intervals ranged from 5 to 8 days. Crop oil concentrate or non-ionic surfactant was added to all spray mixtures. Single control and duplicate treated samples of soybean (forage, hay, and seed) were harvested from each plot on the day of the last application (0 DALA) for forage and hay and 11-17 DALA for seed.

Samples of soybean forage, hay, and seed were analyzed for residues of difenoconazole using modified method Syngenta REM 147.08, "Residue Method for the Determination of Residues of Difenoconazole (CGA-169374) in Various Crops and Processed Crop Fractions" using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Additionally, residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) were measured using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". The limit of quantitation (LOQ) was 0.01 ppm for each analyte in all matrices. The methods were adequate for data collection based on concurrent method recoveries.

The maximum storage duration from harvest to extraction for difenoconazole was 189 days (6.2 months) for soybean forage, 191 days (6.3 months) for soybean hay, and 155 days (5.1 months) for soybean seed. The maximum storage duration from harvest to extraction for the triazole metabolites was 169 days (5.6 months) for soybean forage, 210 days (6.9 months) for soybean hay, and 164 days (5.4 months) for soybean seed. All samples were analyzed within 11 days of extraction; seed samples analyzed for residues of difenoconazole *per se* were analyzed within 6 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of soybean seed, forage, and hay samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted soybean field trial data.

Following two broadcast applications of difenoconazole at a total rate of 0.2146-0.2293 lb ai/A, difenoconazole residues were 5.2-14.3 ppm in/on soybean forage (0 DALA), 8.64-51.8 ppm in/on soybean hay (0 DALA), and <0.01-0.152 ppm in/on soybean seed (11-17 DALA). Samples were also analyzed for T, TA, and TAA with the following residues: <u>T</u>: <0.01 ppm in/on all samples of soybean forage, hay, and seed; <u>TA</u>: <0.01-0.0755 ppm in/on soybean forage, <0.01-0.158 ppm in/on soybean hay, and 0.0295-0.282 ppm in/on soybean seed; and <u>TAA</u>: <0.01-0.013 ppm in/on soybean forage, <0.01-0.0515 ppm in/on soybean hay, and <0.01-0.020 ppm in/on soybean seed.

At two trial sites (NC and IA), samples of soybean forage and hay were taken at 0, 3, 7, and 14 days PHI and samples of soybean seed were taken at 0, 7, 14, 20-21, and 28-33 DALA to assess residue decline. At all trial sites, difenoconazole residues in/on soybean (forage, hay, and straw) declined steadily from 0 DALA to longer post-treatment intervals. Residues of difenoconazole *per se* in/on soybean seeds declined only slightly between 14 DALA and 28-33 DALA.

<u>STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS</u>:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP#378829].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: soil characterization, weather data, maintenance chemical applications, irrigation practices, field history records, tank mix storage stability data, and field samples weights were not collected under GLP. These deviations did not impact the validity of the study.

A. BACKGROUND INFORMATION

Difenoconazole is a broad-spectrum fungicide which belongs to the triazole (including the conazole) class of chemicals. It was developed under the code number CGA-169374.

The chemical structure and nomenclature of difenoconazole and the triazole metabolites are presented in Table A.1. The physicochemical properties of the technical grade of difenoconazole are presented in Table A.2.

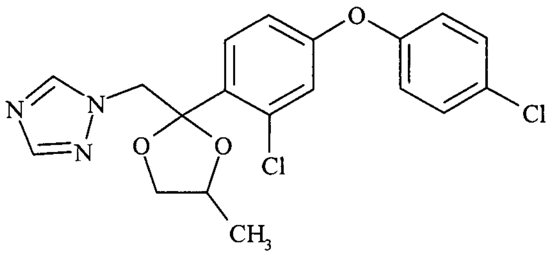
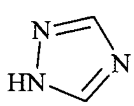
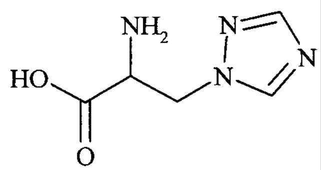
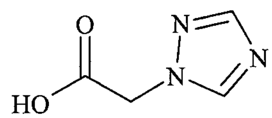
TABLE A.1. Test Compound Nomenclature.			
Compound			
Common name	Difenoconazole		
Company experimental name	CGA-169374		
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole		
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole		
CAS registry number	119446-68-3		
End-use product (EP)	Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole (Inspire®; EPA Reg. No. 100-1262)		
Compound			
Chemical name	Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

TABLE A.2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	
Solvent solubility	<u>g/100 mL at 25 °C</u>: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5 x 10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, Log(K_{OW})	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

B. EXPERIMENTAL DESIGN

Twenty-one field trials were conducted on soybeans in NAFTA Zones 2 (NC; 2 trials), 4 (MO and LA; 3 trials), and 5 (MO, WI, ND, NE, IA, and MN; 16 trials) during 2008 (Table B.1.1). The Gardner, ND trial was only conducted at an exaggerated rate to evaluate processing; results are recorded in a separate DER. The plots received two foliar broadcast applications, at 5 to 8 day retreatment intervals, of the 250EC formulation of difenoconazole. Each application was made at a rate of 0.1060-0.1179 lb ai/A for a total seasonal application rate of 0.2146-0.2293 lb ai/A. Applications were made using backpack or tractor sprayers and a spray volume of ~2 to 47 gal/A. Crop oil concentrate or non-ionic surfactant was added to all spray mixtures.

B.1. Study Site Information

TABLE B.1.1 Trial Site Conditions.

Trial Identification: City, State; Year (Trial No.)	Soil characteristics			
	Type	%OM	pH	CEC meq/100 g
Seven Springs, NC; 2008 (E10NC081261)	Loamy sand	0.7	6.4	6.5
Seven Springs, NC; 2008 (E10NC081262)	Sandy loam	0.9	6.0	6.8
Fisk, MO; 2008 (C23MO081263)	Silt loam	1.7	6.3	5.0
Washington, LA; 2008 (E18LA081264)	Silt loam	1.8	5.4	16.4
Washington, LA; 2008 (E18LA081265)	Silt loam	1.8	5.4	16.4
Oregon, MO; 2008 (C19MO081266)	Silt loam	1.8	6.4	14.9
St. Joseph, MO; 2008 (C19MO081267)	Silty clay loam	2.2	6.9	19.1
Dunn, WI; 2008 (C08WI081268)	Silt loam	3.0	5.5	8
Fitchburg, WI; 2008 (C08WI081269)	Silt loam	2.2	6.6	12
Northwood, ND; 2008 (C13ND081270)	Loam	4.0	7.3	25.8
York, NE; 2008 (E13NE081271)	Silt loam	2.9	6.8	18
Osceola, NE; 2008 (E13NE081272)	Silt loam	3.4	5.9	21
Berkley, IA; 2008 (C30IA081273)	Sandy clay loam	2.5	7.5	14.9
Bagley, IA; 2008 (C30IA081274)	Loam	3.2	6.1	15.1
Lime Springs, IA; 2008 (E19IA081275)	Sandy loam	7.3	7.6	29.1
Lime Springs, IA; 2008 (E19IA081276)	Loam	3.9	7.1	24.0
Richland, IA; 2008 (C18IA081277)	Silty clay loam	4.88	6.53	23.7
Hedrick, IA; 2008 (C18IA081278)	Silty clay loam	4.2	6.75	19.9
Gardner, ND; 2008 (C12MN081279)	Clay loam	3.6	7.8	30.5
Perley, MN; 2008 (C12MN081280)	Silty clay	5.6	7.4	32.8
Gardner, ND; 2008 (C12ND081281)[1]	Clay loam	3.6	7.8	30.5

[1] This trial was only conducted at an exaggerated treatment rate (5x) for processed commodities.

Maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. The crop varieties grown are identified in Table C.3. The actual temperature and rainfall data were reported and no unusual weather conditions were noted during the field trials. Temperature and rainfall were within average historic values for the trial period.

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants
		Method; Timing (Crop growth stage)[2]	Volume (gal/A)[3]	Rate (lb ai/A)	RTI[4] (days)	Total Rate (lb ai/A)	
Soybean Forage and Hay Trials							
Seven Springs, NC; 2008 (E10NC081261)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 69	15.64	0.1131	-	0.2238	COC at 0.516% v/v
		2. Post foliar broadcast; BBCH 71	15.18	0.1107	7		COC at 0.52% v/v
Seven Springs, NC; 2008 (E10NC081262)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 71	15.31	0.1122	-	0.2200	COC at 0.233% v/v
		2. Post foliar broadcast; BBCH 71	15.64	0.1078	5		COC at 0.219% v/v
Fisk, MO; 2008 (C23MO081263)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 67; flowering finishing	2.01	0.1106	-	0.2205	NIS at 0.25% v/v
		2. Post foliar broadcast; BBCH 69	2.00	0.1099	7		NIS at 0.25% v/v
Washington, LA; 2008 (E18LA081264)	Difenoconazole 250 EC	1. Post foliar broadcast; R4	16.46	0.1148	-	0.2253	NIS at 0.25% v/v
		2. Post foliar broadcast; BBCH 71	19.07	0.1105	7		NIS at 0.25% v/v
Washington, LA; 2008 (E18LA081265)	Difenoconazole 250 EC	1. Post foliar broadcast; R3	16.95	0.1124	-	0.2264	NIS at 0.25% v/v
		2. Post broadcast spray; Post foliar broadcast; BBCH 71	19.68	0.1140	7		NIS at 0.25% v/v
Oregon, MO; 2008 (C19MO081266)	Difenoconazole 250 EC	1. Post foliar broadcast; R3	16.21	0.1089	-	0.2154	COC at 1% v/v
		2. Post foliar broadcast; R4	16.46	0.1065	7		COC at 1% v/v
St. Joseph, MO; 2008 (C19MO081267)	Difenoconazole 250 EC	1. Post foliar broadcast; R3	17.14	0.1099	-	0.2207	COC at 1% v/v
		2. Post foliar broadcast; R4	16.69	0.1108	8		COC at 1% v/v
Dunn, WI; 2008 (C08WI081268)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 73	29.28	0.1086	-	0.2146	NIS at 0.127% v/v
		2. Post foliar broadcast; BBCH 75	27.40	0.1060	7		NIS at 0.123% v/v

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants
		Method; Timing (Crop growth stage)[2]	Volume (gal/A)[3]	Rate (lb ai/A)	RTI[4] (days)	Total Rate (lb ai/A)	
Fitchburg, WI; 2008 (C08WI081269)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 71	28.73	0.1118	-	0.2234	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 74	28.48	0.1116	7		NIS at 0.125% v/v
Northwood, ND; 2008 (C13ND081270)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 71	18.71	0.1102	-	0.2194	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 73	19.87	0.1092	7		NIS at 0.125% v/v
York, NE; 2008 (E13NE081271)	Difenoconazole 250 EC	1. Post foliar broadcast; R3	19.58	0.1091	-	0.2177	NIS at 0.25% v/v
		2. Post foliar broadcast; R4	19.66	0.1086	7		NIS at 0.25% v/v
Osceola, NE; 2008 (E13NE081272)	Difenoconazole 250 EC	1. Post foliar broadcast; R3	19.74	0.1100	-	0.2191	NIS at 0.25% v/v
		2. Post foliar broadcast; R3	19.76	0.1091	7		NIS at 0.25% v/v
Berkley, IA; 2008 (C30IA081273)	Difenoconazole 250 EC	1. Post foliar broadcast; 65	14.34	0.1091	-	0.2203	NIS at 0.25% v/v
		2. Post foliar broadcast; 65	15.47	0.1112	7		NIS at 0.25% v/v
Bagley, IA; 2008 (C30IA081274)	Difenoconazole 250 EC	1. Post foliar broadcast; 69	15.00	0.1179	-	0.2285	NIS at 0.25% v/v
		2. Post foliar broadcast; 69	13.35	0.1106	7		NIS at 0.25% v/v
Lime Springs, IA; 2008 (E19IA081275)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 77	46.98	0.1125	-	0.2256	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 79	47.23	0.1131	7		NIS at 0.125% v/v
Lime Springs, IA; 2008 (E19IA081276)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 77	46.81	0.1121	-	0.2245	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 79	46.97	0.1124	7		NIS at 0.125% v/v
Richland, IA; 2008 (C18IA081277)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 67; R3	17.32	0.1156	-	0.2267	NIS at 0.25% v/v
		2. Post foliar broadcast; 70	17.93	0.1111	7		NIS at 0.25% v/v

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants
		Method; Timing (Crop growth stage)[2]	Volume (gal/A)[3]	Rate (lb ai/A)	RTI[4] (days)	Total Rate (lb ai/A)	
Hedrick, IA; 2008 (C18IA081278)	Difenoconazole 250 EC	1. Post foliar broadcast; 72	17.80	0.1086	-	0.2250	NIS at 0.25% v/v
		2. Post foliar broadcast; BBCH 73	15.93	0.1164	7		NIS at 0.25% v/v
Gardner, ND; 2008 (C12MN081279)	Difenoconazole 250 EC	1. Post foliar broadcast; 65	15.42	0.1135	-	0.2293	NIS at 0.2% v/v
		2. Post foliar broadcast; BBCH 70	15.75	0.1158	7		NIS at 0.2% v/v
Perley, MN; 2008 (C12MN081280)	Difenoconazole 250 EC	1. Post foliar broadcast; 65	15.20	0.1119	-	0.2266	NIS at 0.2% v/v
		2. Post foliar broadcast; BBCH 75	15.61	0.1147	7		NIS at 0.2% v/v
Soybean Seed Trials							
Seven Springs, NC; 2008 (E10NC081261)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 88	28.88	0.1107	-	0.2233	COC at 0.243% v/v
		2. Post foliar broadcast; BBCH 88	16.93	0.1126	7		COC at 0.35% v/v
Seven Springs, NC; 2008 (E10NC081262)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 93	16.42	0.1100	-	0.2209	COC at 0.319% v/v
		2. Post foliar broadcast; BBCH 88	16.03	0.1109	7		COC at 0.329% v/v
Fisk, MO; 2008 (C23MO081263)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 81	2.02	0.1111	-	0.2217	NIS at 0.25% v/v
		2. Post foliar broadcast; BBCH 87	2.01	0.1106	6		NIS at 0.25% v/v
Washington, LA; 2008 (E18LA081264)	Difenoconazole 250 EC	1. Post foliar broadcast; 82	20.17	0.1116	-	0.2227	NIS at 0.25% v/v
		2. Post foliar broadcast; 85	18.20	0.1111	7		NIS at 0.25% v/v
Washington, LA; 2008 (E18LA081265)	Difenoconazole 250 EC	1. Post foliar broadcast; 82	20.06	0.1110	-	0.2209	NIS at 0.25% v/v
		2. Post foliar broadcast; 85	18.00	0.1099	7		NIS at 0.25% v/v
Oregon, MO; 2008 (C19MO081266)	Difenoconazole 250 EC	1. Post foliar broadcast; R6	16.11	0.1096	-	0.2228	COC at 1% v/v
		2. Post foliar broadcast; late R6, early R7	17.04	0.1132	7		COC at 1% v/v

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants
		Method; Timing (Crop growth stage)[2]	Volume (gal/A)[3]	Rate (lb ai/A)	RTI[4] (days)	Total Rate (lb ai/A)	
St. Joseph, MO; 2008 (C19MO081267)	Difenoconazole 250 EC	1. Post foliar broadcast; R5	16.95	0.1126	-	0.2234	COC at 1% v/v
		2. Post foliar broadcast; R6	16.68	0.1108	7		COC at 1% v/v
Dunn, WI; 2008 (C08WI081268)	Difenoconazole 250 EC	1. Post foliar broadcast; 75	31.67	0.1110	-	0.2244	NIS at 0.126% v/v
		2. Post foliar broadcast; 81	30.56	0.1134	7		NIS at 0.127% v/v
Fitchburg, WI; 2008 (C08WI081269)	Difenoconazole 250 EC	1. Post foliar broadcast; 74	31.12	0.1089	-	0.2197	NIS at 0.125% v/v
		2. Post foliar broadcast; 80	28.48	0.1108	7		NIS at 0.125% v/v
Northwood, ND; 2008 (C13ND081270)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 82	29.99	0.1100	-	0.2214	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 88	30.36	0.1114	7		NIS at 0.125% v/v
York, NE; 2008 (E13NE081271)	Difenoconazole 250 EC	1. Post foliar broadcast; 93	19.12	0.1099	-	0.2212	NIS at 0.25% v/v
		2. Post foliar broadcast; 95-97	19.01	0.1113	8		NIS at 0.25% v/v
Osceola, NE; 2008 (E13NE081272)	Difenoconazole 250 EC	1. Post foliar broadcast; 93-95	19.08	0.1098	-	0.2209	NIS at 0.25% v/v
		2. Post foliar broadcast; 95	19.28	0.1110	7		NIS at 0.25% v/v
Berkley, IA; 2008 (C30IA081273)	Difenoconazole 250 EC	1. Post foliar broadcast; 79	12.40	0.1079	-	0.2199	NIS at 0.27% v/v
		2. Post foliar broadcast; 95	12.62	0.1120	7		NIS at 0.2% v/v
Bagley, IA; 2008 (C30IA081274)	Difenoconazole 250 EC	1. Post foliar broadcast; 93	12.22	0.1079	-	0.2175	NIS at 0.2% v/v
		2. Post foliar broadcast; 95	13.30	0.1096	7		NIS at 0.25% v/v
Lime Springs, IA; 2008 (E19IA081275)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 86	46.56	0.1115	-	0.2226	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 88	46.42	0.1111	7		NIS at 0.125% v/v

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants
		Method; Timing (Crop growth stage)[2]	Volume (gal/A)[3]	Rate (lb ai/A)	RTI[4] (days)	Total Rate (lb ai/A)	
Lime Springs, IA; 2008 (E19IA081276)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 86	45.64	0.1093	-	0.2188	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 88	45.75	0.1095	7		NIS at 0.125% v/v
Richland, IA; 2008 (C18IA081277)	Difenoconazole 250 EC	1. Post foliar broadcast; 79	18.96	0.1107	-	0.2218	NIS at 0.25% v/v
		2. Post foliar broadcast; BBCH 83	18.46	0.1111	7		NIS at 0.25% v/v
Hedrick, IA; 2008 (C18IA081278)	Difenoconazole 250 EC	1. Post foliar broadcast; 79	16.67	0.1097	-	0.2200	NIS at 0.25% v/v
		2. Post foliar broadcast; BBCH 95	18.32	0.1103	7		NIS at 0.25% v/v
Gardner, ND; 2008 (C12MN081279)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 85	18.63	0.1134	-	0.2237	NIS at 0.2% v/v
		2. Post foliar broadcast; 87	20.20	0.1103	7		NIS at 0.2% v/v
Perley, MN; 2008 (C12MN081280)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 85	19.03	0.1158	-	0.2237	NIS at 0.2% v/v
		2. Post foliar broadcast; BBCH 89	19.77	0.1079	7		NIS at 0.2% v/v

1 EP = End-use Product; Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal ifenoconazole.
2 Difenoconazole was applied to forage/hay at 7 days prior to harvest for the first application and on the day of harvest at the second application. Difenoconazole was applied to seeds 21 days prior to harvest for the first application and 14 days prior to harvest for the second application.
3 Gallons per acre.
4 Retreatment Interval.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Soybean		
	Submitted[1]	Requested	
		Canada	U.S.
1	--	NA	--
1A	--	NA	--
2	2	NA	2
3	--	NA	--
4	3	NA	3
5	16	NA	15
5A	--	NA	--
5B	--	NA	--
6	--	NA	--
7	--	NA	--

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Soybean		
	Submitted[1]	Requested	
		Canada	U.S.
7A	--	NA	--
8	--	NA	--
9	--	NA	--
10	--	NA	--
11	--	NA	--
12	--	NA	--
13	--	NA	--
14	--	NA	--
15	--	NA	--
16	--	NA	--
17	--	NA	--
18	--	NA	--
19	--	NA	--
20	--	NA	--
21	--	NA	--
Total	21[1]		20

[1] One Region 5 trial site was only conducted at an exaggerated rate in order to examine residues in processed commodities.

B.2. Sample Handling and Preparation

Single control and duplicate treated samples of soybean forage were collected on the day of the last application. Soybean plants were cut 0 days after the last application (DALA) and allowed to dry for 2-11 days to produce hay samples. Single control and duplicate treated samples of mature soybean seed were collected at approximately 14 DALA. At two trial sites (NC and IA), additional single samples of soybean forage and hay were taken at 3, 7, and 14 DALA to assess residue decline. The hay samples were allowed to dry for 3-6 days to produce the residue decline samples. In addition, at two trial sites, additional single samples of mature soybean seed were collected at 0, 7, 20 or 21, and 28 or 33 DALA to assess residue decline.

Samples were shipped frozen to the preparation facility, where they were stored at <-10°C until sample preparation. The forage and hay samples were cut into small pieces and ground with dry ice in a Hobart foodcutter. Seed samples were ground in a table-top mill. Following preparation, samples were returned to frozen storage and shipped frozen to the analytical laboratory (Morse Laboratories, LLC; Sacramento, CA).

B.3. Analytical Methodology

Samples of soybean forage, hay, and seed were analyzed for residues of difenoconazole with modified analytical method Syngenta REM 147.08 titled "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS". Samples of soybean forage, hay, and seed were analyzed for residues of difenoconazole triazole metabolites 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) with modified analytical method Morse Laboratories, Inc. Analytical Method No. 160 Revision 2 titled "Determination of 1,2,4-Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". Both methods have been reviewed previously by HED (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan). Brief descriptions of the methods were included in the submission.

Residues of difenoconazole in soybean samples were extracted by refluxing with methanol/concentrated ammonium hydroxide (80:20, v:v). Aliquots of the extracts were diluted with ultra-pure water, cleaned up using solid phase extraction, and analyzed using high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). Residues of metabolites T, TA, and TAA were extracted with methanol/water (80:20, v/v). Following the addition of Celite, the extracts were vacuum filtered, rinsed, and brought to volume with methanol/water (80:20, v:v). Aliquots of the TAA extract were purified by solid phase extraction and then derivatized by HCl/butanol esterification. The TA aliquot underwent two derivatizations: an esterification using HCL/butanol and an acylation using heptafluoro butyric anhydride (HFBA). The T aliquot was directly derivatized with dansyl chloride to produce the dansyl derivative of 1,2,4-triazole and partitioned into ethyl acetate. All metabolite extracts were then evaporated to dryness, redissolved in acetonitrile/water (30:70, v/v), and analyzed using HPLC with mass spectrometric (MS/MS) detection.

The LOQ was 0.01 ppm for difenoconazole in all soybean matrices; the corresponding LOD was 0.000125 ppm. The LOQ (as respective parent equivalents) was 0.01 ppm for the triazole metabolites T, TA, and TAA. The LOD was 0.00003 ppm for T and TA and 0.00005 ppm for TAA in all soybean matrices.

The methods were validated in conjunction with the analysis of field trial samples. For concurrent recoveries of difenoconazole, control samples of forage were fortified at 0.01, 0.10, and 20 ppm, control samples of hay were fortified at 0.01, 0.10, 5.0, and 60 ppm, and control samples of seed were fortified at 0.01, 0.10, 5.0, and 10 ppm. For concurrent recoveries of the triazole metabolite T, control samples of forage and hay were fortified at 0.01 and 0.1 ppm and control samples of seed were fortified at 0.01, 0.1, and 0.5 ppm. For concurrent recoveries of the triazole metabolite TA, control samples of forage were fortified at 0.01, 0.08, 0.1 and 0.8 ppm, control samples of hay were fortified at 0.015, 0.025, 0.25, 0.5, and 2.5 ppm, and control samples of seed were fortified at 0.1, 0.25, 0.5, and 2.5 ppm. For concurrent recoveries of the triazole metabolite TAA, control samples of forage were fortified at 0.01 and 0.10 ppm, control samples of hay were fortified at 0.01, 0.02, 0.1, and 0.2 ppm, and control samples of seed were fortified at 0.01, 0.10, and 0.5 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations for samples of soybean matrices are reported in Table C.2. Difenoconazole samples were stored at <-10 °C prior to extraction for analysis for 97-189 days (3.2-6.2 months) for soybean forage, 97-191 days (3.2-6.3 months) for soybean hay, and 71-155 days (2.3-5.1 months) for soybean seed and triazole metabolite samples were stored for 91-169 days (3.0-5.6 months) for soybean forage, 97-210 days (3.2-6.9 months) for soybean hay, and 67-164 days (2.2-5.4 months) for soybean seed. All samples were analyzed within 11 days of extraction; seed samples analyzed for residues of difenoconazole *per se* were analyzed within 6 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of soybean seed, forage, and hay samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted soybean field trial data.

Concurrent method recovery data are presented in Table C.1. The modified LC/MS-MS methods (Syngenta REM 147.08 and Morse Laboratories, Inc. Analytical Method No. 160 Revision 2) used for determining residues of difenoconazole and the triazole metabolites T, TA, and TAA in/on soybean (forage, hay, and seed) were adequately validated in conjunction with the analysis of field trial samples. Concurrent recoveries were within the acceptable range of 70-120% with two exceptions: at the 0.01 ppm spike level, recovery of 64% for difenoconazole in forage and at the 0.10 ppm spike level, recovery of 122% for T in seed. However, all mean recoveries were within the acceptable range.

Apparent residues of difenoconazole were below the LOQ (<0.01 ppm) in/on samples of untreated soybean forage (n = 24), soybean hay (n = 22), and soybean seed (n = 30). Quantifiable apparent residues of difenoconazole were observed in/on two samples of untreated soybean forage (0.01 and 0.02 ppm), four samples of soybean hay (0.01-6.9 ppm), and one sample of untreated soybean seed (0.05 ppm). Apparent residues of 1,2,4-T were below the LOQ (<0.01 ppm) in/on all samples of untreated soybean forage (n=26), soybean hay (n=26), and soybean seed (n=26). Apparent residues of TA were below the LOQ (<0.01 ppm) in/on samples of untreated soybean forage (n = 6) and soybean hay (n = 2). Quantifiable apparent residues of TA were observed in/on 20 samples of untreated soybean forage (0.01-0.08 ppm), 24 samples of soybean hay (0.01-0.12 ppm), and all samples (n = 31) of untreated soybean seed (0.04-0.60 ppm). Apparent residues of TAA were below the LOQ (<0.01 ppm) in/on samples of untreated soybean forage (n=26), soybean hay (n=20), and soybean seed (n=27). Quantifiable apparent residues of TAA were observed in/on six samples of soybean hay (0.01-0.03 ppm) and four samples of untreated soybean seed (0.01-0.03 ppm). The petitioner attributed the occurrence of residues of TA and TAA in/on untreated samples to the widespread use of triazoles and the non-specific nature of the common moiety method of analysis. Adequate example chromatograms were provided.

Residue data from the soybean field trials are reported in Table C.3. A summary of residue data for soybean is presented in Table C.4.

Following two foliar broadcast treatment applications of difenoconazole at a total rate of 0.2146-0.2293 lb ai/A, difenoconazole residues were 5.24-14.3 ppm in/on soybean forage (0 DALA), 8.64-51.8 ppm in/on soybean hay (0 DALA), and <0.01-0.152 ppm in/on soybean seed (11-17 DALA). Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of soybean forage, hay, and seed; TA: <0.01-0.0755 ppm in/on soybean forage, <0.01-0.158 ppm in/on soybean hay, and 0.0295-0.282 ppm in/on soybean seed; and TAA: <0.01-0.013 ppm in/on soybean forage, <0.01-0.0515 ppm in/on soybean hay, and <0.01-0.020 ppm in/on soybean seed.

In the Seven Springs, NC residue decline trial, difenoconazole residues declined steadily from 0 DALA to longer post-treatment intervals in/on soybean forage, hay, and seed (Figure C.1.1). For soybean forage, difenoconazole residues declined from 8.18 ppm (mean) at 0 DALA to 3.82 ppm by 14 DALA. For soybean hay, difenoconazole residues declined from 29.3 ppm (mean) at 0 DALA to 9.8 ppm at 14 DALA. For soybean seed, residues of difenoconazole *per se* declined from 0.0436 ppm (mean) at 0 DALA to <0.01 ppm by 28 DALA but declined could not be measured between 14 DALA and 28 DALA (residues were <0.01 ppm at both intervals).

In the Bagley, IA residue decline trial, difenoconazole residues declined steadily from 0 DALA to longer post-treatment intervals in/on soybean forage, hay, and seed (Figure C.1.2). For soybean forage, difenoconazole residues declined from 8.64 ppm (mean) at 0 DALA to 1.46 ppm by 14 DALA. For soybean hay, difenoconazole residues declined from 16 ppm (mean) at 0 DALA to 7.4 ppm at 14 DALA. For soybean seed, residues of difenoconazole *per se* declined from 0.0708 ppm at 0 DALA to 0.0164 ppm by 33 DALA but showed little decline between 14 DALA (0.0187 ppm) and 33 DALA (0.0164 ppm).

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Soybean Matrices.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)[1]
Forage	Difenoconazole	0.01	10	64, 74, 76, 91, 70, 70, 76, 88, 95, 88	79 ± 10
		0.10	9	76, 78, 82, 93, 72, 71, 91, 102, 94	84 ± 11
		20	1	118	NA
	1,2,4-Triazole	0.01	9	104, 92, 97, 95, 102, 77, 80, 88, 108	94 ± 11
		0.10	9	98, 90, 96, 95, 95, 91, 91, 100, 90	94 ± 4
	Triazole Acetic Acid	0.01	9	95, 96, 89, 95, 93, 99, 104, 97, 87	95 ± 5
		0.10	9	94, 97, 90, 99, 92, 96, 96, 89, 86	93 ± 4
	Triazole Alanine	0.01	5	87, 97, 98, 86, 72	88 ± 11
		0.08	4	94, 82, 87, 102	91 ± 9
		0.1	5	89, 89, 85, 88, 87	88 ± 2
		0.8	4	91, 83, 88, 94	89 ± 5
Hay	Difenoconazole	0.01	9	70, 70, 73, 92, 79, 88, 91, 98, 80	82 ± 10
		0.10	7	75, 78, 94, 71, 85, 80, 100	83 ± 10
		5.0	1	101	NA
		60	1	108	NA
	1,2,4-Triazole	0.01	8	84, 93, 86, 97, 95, 92, 108, 72	91 ± 11
		0.10	8	105, 90, 92, 82, 94, 86, 76, 89	89 ± 9
	Triazole Acetic Acid	0.01	7	92, 91, 86, 109, 88, 75, 84	89 ± 10
		0.02	1	92	NA
		0.10	7	95, 93, 80, 88, 82, 81, 90	87 ± 6
		0.20	1	89	NA
	Triazole Alanine	0.015	1	91	NA
		0.025	9	80, 85, 80, 70, 82, 70, 78, 80, 86	79 ± 6
		0.25	8	76, 76, 71, 74, 72, 73, 71, 77	74 ± 2
		0.5	2	76, 77	77
		2.5	1	77	NA
Seed	Difenoconazole	0.01	11	101, 95, 94, 104, 70, 94, 106, 110, 100, 113, 93	98 ± 12
		0.10	9	98, 90, 102, 78, 98, 110, 117, 97, 99	99 ± 11
		5	1	108	NA
		10	1	116	NA
	1,2,4-Triazole	0.01	12	100, 79, 107, 89, 104, 93, 84, 80, 77, 95, 82, 77	89 ± 11
		0.10	10	96, 85, 122, 89, 77, 87, 84, 88, 96, 97	92 ± 12
		0.5	2	98, 99	99

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Soybean Matrices.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)[1]
	Triazole Acetic Acid	0.01	12	98, 101, 83, 86, 105, 104, 83, 101, 98, 105, 105, 96	97 ± 8
		0.10	10	99, 104, 93, 93, 88, 102, 107, 104, 106, 96	99 ± 6
		0.5	2	102, 107	105
	Triazole Alanine	0.10	10	86, 71, 103, 112, 84, 100, 77, 102, 80, 92	91 ± 13
		0.25	2	90, 83	87
		0.5	10	87, 78, 101, 97, 89, 89, 78, 102, 97, 94	91 ± 9
		2.5	2	84, 86	85

[1] Standard deviations were calculated only for fortification levels having ≥3 samples.

TABLE C.2. Summary of Storage Conditions.

Matrix	Analyte	Storage Temperature (°C)	Actual Storage Duration[1]	Limit of Demonstrated Storage Stability[2]
Soybean, forage	Difenoconazole	<-10	97-189 days (3.2-6.2 months)	None provided with the subject submission; however, based on previously submitted storage stability data (DP#s 340379 and 356135), when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable at -20°C for up to two years in/on cotton seed, cotton oil, and cotton meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw.
	Triazole metabolites (T, TA, TAA)		91-169 days (3.0-5.6 months)	
Soybean, hay	Difenoconazole		97-191 days (3.2-6.3 months)	
	Triazole metabolites (T, TA, TAA)		97-210 days (3.2-6.9 months)	
Soybean, seed	Difenoconazole		71-155 days (2.3-5.1 months)	
	Triazole metabolites (T, TA, TAA)		67-164 days (2.2-5.4 months)	None provided with the subject study; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016).

[1] Interval from harvest to extraction for analysis. Extracts were stored 0-11 days prior to analysis. Soybean seed extracts analyzed for difenoconazole *per se* were stored up to 6 days prior to analysis.

TABLE C.3. Residue Data from Soybean Field Trials with Difenoconazole.

Trial ID (City, State; Year)	Zone	Crop/ Variety	EP[1]	Total Rate (lb ai/A)	DALA	Residues (ppm)[2]			
						Difenoconazole	T	TA	TAA
Soybean forage									
Seven Springs, NC; 2008 (E10NC081261)[3]	2	Soybean/DKB 64-51 (SE74480)	Difenoconazole 250EC	0.2238	0	8.61 7.74	ND ND	0.0134 0.0186	<0.01 <0.01
					3	6.48	ND	0.0232	<0.01
					6	7.15	ND	0.0266	<0.01
					14	3.82	ND	0.0412	0.0138
Seven Springs, NC; 2008 (E10NC081262)	2	Soybean/ 95M50	Difenoconazole 250EC	0.2200	0	6.30 6.26	ND ND	0.0305 0.0356	<0.01 <0.01
Fisk, MO; 2008 (C23MO081263)	4	Soybean/ Armor 47G7	Difenoconazole 250EC	0.2205	0	11.5 11.2	ND ND	0.0252 0.0216	<0.01 <0.01
Washington, LA; 2008 (E18LA081264)	4	Soybean/ AG5605	Difenoconazole 250EC	0.2253	0	7.76 7.32	ND ND	0.0284 0.0146	<0.01 <0.01
Washington, LA; 2008 (E18LA081265)	4	Soybean/ AG5605	Difenoconazole 250EC	0.2264	0	5.24 5.84	ND ND	0.0284 0.0325	<0.01 <0.01
Oregon, MO; 2008 (C19MO81266)	5	Soybean/ Pioneer 93M11	Difenoconazole 250EC	0.2154	0	12.2 13.1	ND ND	<0.01 <0.01	<0.01 <0.01
St. Joseph, MO; 2008 (C19MO081267)	5	Soybean/ Pioneer 93M96	Difenoconazole 250EC	0.2207	0	10.8 6.72	ND ND	<0.01 <0.01	<0.01 <0.01
Dunn, WI; 2008 (C08WI081268)	5	Soybean/ S17-A1	Difenoconazole 250EC	0.2146	0	5.60 5.88	ND ND	0.0182 0.0274	<0.01 <0.01
Fitchburg, WI; 2008 (C08WI081269)	5	Soybean/ S19-V2	Difenoconazole 250EC	0.2234	0	7.71 6.77	ND ND	0.0268 0.0279	<0.01 <0.01
Northwood, ND; 2008 (C13ND081270)	5	Soybean/ Asgrow AG0202	Difenoconazole 250EC	0.2194	0	9.44 9.96	ND ND	0.0274 0.0260	<0.01 <0.01
York, NE; 2008 (E13NE081271)	5	Soybean/ NC + 2A46RR	Difenoconazole 250EC	0.2177	0	6.83 11.4	ND ND	0.0186 0.0148	<0.01 <0.01
Osceola, NE; 2008 (E13NE081272)	5	Soybean/ NC + 2A46RR	Difenoconazole 250EC	0.2191	0	10.3 7.84	ND ND	0.0282 0.0245	<0.01 <0.01
Berkley, IA; 2008 (C30IA081273)	5	Soybean/ 93M11	Difenoconazole 250EC	0.2203	0	10.9 9.16	ND ND	0.0110 0.0104	<0.01 <0.01
Bagley, IA; 2008 (C30IA081274)[3]	5	Soybean/ 93M11	Difenoconazole 250EC	0.2285	0	9.60 7.68	ND ND	0.0189 0.0206	<0.01 <0.01
					3	5.72	ND	0.0188	<0.01
					7	4.40	ND	0.0269	<0.01
					14	1.46	ND	0.0251	<0.01
Lime Springs, IA; 2008 (E19IA081275)	5	Soybean/ 5726085	Difenoconazole 250EC	0.2256	0	9.34 10.0	ND ND	0.0158 0.0151	<0.01 <0.01
Lime Springs, IA; 2008 (E19IA081276)	5	Soybean/ 5726085	Difenoconazole 250EC	0.2245	0	7.30 8.65	ND ND	0.0248 0.0177	<0.01 <0.01
Richland, IA; 2008 (C18IA081277)	5	Soybean/ Pioneer 93M11	Difenoconazole 250EC	0.2267	0	9.88 13.1	ND ND	0.0115 0.0134	<0.01 <0.01

TABLE C.3. Residue Data from Soybean Field Trials with Difenoconazole.

Trial ID (City, State; Year)	Zone	Crop/ Variety	EP[1]	Total Rate (lb ai/A)	DALA	Residues (ppm)[2]			
						Difenoconazole	T	TA	TAA
Hedrick, IA; 2008 (C18IA081278)	5	Soybean/ 93M11	Difenoconazole 250EC	0.2250	0	5.20 7.08	ND ND	0.0376 0.0324	<0.01 <0.01
Gardner, ND; 2008 (C12MN081279)	5	Soybean/ 5B077RR	Difenoconazole 250EC	0.2293	0	13.4 10.1	<0.01 ND	0.0630 0.0630	<0.01 <0.01
Perley, MN; 2008 (C12MN081280)	5	Soybean/ 5A009RR	Difenoconazole 250EC	0.2266	0	14.3 13.5	ND ND	0.0675 0.0755	0.0108 0.0130
Soybean hay									
Seven Springs, NC; 2008 (E10NC081261)[3]	2	Soybean/D KB 64-51 (SE74480)	Difenoconazole 250EC	0.2238	0	31.2 27.4	<0.01 <0.01	0.0350 0.0289	0.0192 0.0167
					3	21.3	<0.01	0.0416	0.0230
					6	16.4	ND	0.0486	0.0175
					14	9.80	<0.01	0.0640	0.0363
Seven Springs, NC; 2008 (E10NC081262)	2	Soybean/ 95M50	Difenoconazole 250EC	0.2200	0	13.8 15.3	<0.01 <0.01	0.0530 0.0585	0.0412 0.0482
Fisk, MO; 2008 (C23MO081263)	4	Soybean/ Armor 47G7	Difenoconazole 250EC	0.2205	0	21.4 29.8	<0.01 <0.01	0.0410 0.0515	0.0438 0.0453
Washington, LA; 2008 (E18LA081264)	4	Soybean/ AG5605	Difenoconazole 250EC	0.2253	0	10.3 12.2	ND ND	0.0114 0.0142	0.0116 0.0120
Washington, LA; 2008 (E18LA081265)	4	Soybean/ AG5605	Difenoconazole 250EC	0.2264	0	8.88 8.64	<0.01 ND	0.0253 0.0392	0.0143 0.0135
Oregon, MO; 2008 (C19MO81266)	5	Soybean/ Pioneer 93M11	Difenoconazole 250EC	0.2154	0	33.6 31.3	<0.01 <0.01	0.0244 0.0219	0.0264 0.0222
St. Joseph, MO; 2008 (C19MO081267)	5	Soybean/ Pioneer 93M96	Difenoconazole 250EC	0.2207	0	18.1 25.3	<0.01 ND	0.0289 0.0247	0.0184 0.0180
Dunn, WI; 2008 (C08WI081268)	5	Soybean/ S17-A1	Difenoconazole 250EC	0.2146	0	22.2 13.2	<0.01 <0.01	0.0144 0.0165	<0.01 <0.01
Fitchburg, WI; 2008 (C08WI081269)	5	Soybean/ S19-V2	Difenoconazole 250EC	0.2234	0	16.1 14.6	ND ND	<0.01 0.0128	0.0128 0.0120
Northwood, ND; 2008 (C13ND081270)	5	Soybean/ Asgrow AG0202	Difenoconazole 250EC	0.2194	0	30.2 26.4	<0.01 <0.01	0.0575 0.0460	0.0262 0.0204
York, NE; 2008 (E13NE081271)	5	Soybean/ NC + 2A46RR	Difenoconazole 250EC	0.2177	0	14.7 13.6	ND ND	0.0223 0.0332	<0.01 0.0108
Osceola, NE; 2008 (E13NE081272)	5	Soybean/ NC + 2A46RR	Difenoconazole 250EC	0.2191	0	23.4 24.6	ND ND	0.0525 0.0635	<0.01 0.0107
Berkley, IA; 2008 (C30IA081273)	5	Soybean/ 93M11	Difenoconazole 250EC	0.2203	0	20.0 16.2	<0.01 <0.01	0.0415 0.0378	0.0288 0.0242
Bagley, IA; 2008 (C30IA081274)[3]	5	Soybean/ 93M11	Difenoconazole 250EC	0.2285	0	16.8 15.2	ND ND	0.0365 0.0468	0.0308 0.0283
					3	10.4	ND	0.0472	0.0232
					7	8.56	ND	0.0490	0.0261
					14	7.40	ND	0.0655	0.0310
Lime Springs, IA; 2008 (E19IA081275)	5	Soybean/ 5726085	Difenoconazole 250EC	0.2256	0	25.5 25.7	<0.01 ND	0.0316 0.0318	0.0196 0.0222
Lime Springs, IA; 2008 (E19IA081276)	5	Soybean/ 5726085	Difenoconazole 250EC	0.2245	0	9.12 11.7	ND ND	0.0148 0.0162	0.0122 0.0113

TABLE C.3. Residue Data from Soybean Field Trials with Difenoconazole.

Trial ID (City, State; Year)	Zone	Crop/ Variety	EP[1]	Total Rate (lb ai/A)	DALA	Residues (ppm)[2]			
						Difenoconazole	T	TA	TAA
Richland, IA; 2008 (C18IA081277)	5	Soybean/ Pioneer 93M11	Difenoconazole 250EC	0.2267	0	51.8 34.9	<0.01 <0.01	0.0465 0.0378	0.0272 0.0226
Hedrick, IA; 2008 (C18IA081278)	5	Soybean/ 93M11	Difenoconazole 250EC	0.2250	0	34.6 31.0	<0.01 <0.01	0.0835 0.0760	0.0150 0.0140
Gardner, ND; 2008 (C12MN081279)	5	Soybean/ 5B077RR	Difenoconazole 250EC	0.2293	0	41.6 39.5	<0.01 <0.01	0.124 0.106	0.0434 0.0390
Perley, MN; 2008 (C12MN081280)	5	Soybean/ 5A009RR	Difenoconazole 250EC	0.2266	0	42.1 40.2	<0.01 <0.01	0.158 0.0970	0.0515 0.0465
Soybean seed									
Seven Springs, NC; 2008 (E10NC081261)[3]	2	Soybean/D KB 64-51 (SE74480)	Difenoconazole 250EC	0.2233	0	0.0436	ND	0.204	<0.01
					7	0.0174	ND	0.150	<0.01
					14	<0.01 <0.01	ND ND	0.118 0.133	<0.01 <0.01
					20	<0.01	ND	0.162	<0.01
					28	<0.01	<0.01	0.124	<0.01
Seven Springs, NC; 2008 (E10NC081262)	2	Soybean/ 95M50	Difenoconazole 250EC	0.2209	14	<0.01 <0.01	ND ND	0.0430 0.0461	<0.01 <0.01
Fisk, MO; 2008 (C23MO081263)	4	Soybean/ Armor 47G7	Difenoconazole 250EC	0.2217	14	<0.01 0.0139	ND ND	0.114 0.0895	<0.01 <0.01
Washington, LA; 2008 (E18LA081264)	4	Soybean/ AG5605	Difenoconazole 250EC	0.2227	14	0.0120 0.0194	ND ND	0.0680 0.0374	<0.01 <0.01
Washington, LA; 2008 (E18LA081265)	4	Soybean/ AG5605	Difenoconazole 250EC	0.2209	14	0.0424 0.0384	<0.01 <0.01	0.0890 0.0730	<0.01 <0.01
Oregon, MO; 2008 (C19MO81266)	5	Soybean/ Pioneer 93M11	Difenoconazole 250EC	0.2228	14	0.0121 0.0134	<0.01 ND	0.0835 0.0850	<0.01 <0.01
St. Joseph, MO; 2008 (C19MO081267)	5	Soybean/ Pioneer 93M96	Difenoconazole 250EC	0.2234	17	<0.01 <0.01	ND ND	0.154 0.191	<0.01 <0.01
Dunn, WI; 2008 (C08WI081268)	5	Soybean/ S17-A1	Difenoconazole 250EC	0.2244	14	<0.01 <0.01	ND ND	0.0695 0.0780	<0.01 <0.01
Fitchburg, WI; 2008 (C08WI081269)	5	Soybean/ S19-V2	Difenoconazole 250EC	0.2197	14	0.0258 0.0154	ND ND	0.0855 0.0855	<0.01 <0.01
Northwood, ND; 2008 (C13ND081270)	5	Soybean/ Asgrow AG0202	Difenoconazole 250EC	0.2214	15	<0.01 <0.01	ND ND	0.128 0.110	<0.01 <0.01
York, NE; 2008 (E13NE081271)	5	Soybean/ NC + 2A46RR	Difenoconazole 250EC	0.2212	11	<0.01 <0.01	ND ND	0.129 0.126	<0.01 <0.01
Osceola, NE; 2008 (E13NE081272)	5	Soybean/ NC + 2A46RR	Difenoconazole 250EC	0.2209	13	<0.01 <0.01	ND ND	0.156 0.178	<0.01 <0.01
Berkley, IA; 2008 (C30IA081273)	5	Soybean/ 93M11	Difenoconazole 250EC	0.2199	14	<0.01 <0.01	ND ND	0.0785 0.0770	<0.01 <0.01
Bagley, IA; 2008 (C30IA081274)[3]	5	Soybean/ 93M11	Difenoconazole 250EC	0.2175	0	0.0708	ND	0.0685	<0.01
					7	<0.01	<0.01	0.0820	<0.01
					14	0.0191 0.0183	ND ND	0.0875 0.0920	<0.01 <0.01
					21	<0.01	ND	0.0800	<0.01
					33	0.0164	ND	0.0422	<0.01

TABLE C.3. Residue Data from Soybean Field Trials with Difenoconazole.

Trial ID (City, State; Year)	Zone	Crop/ Variety	EP[1]	Total Rate (lb ai/A)	DALA	Residues (ppm)[2]			
						Difenoconazole	T	TA	TAA
Lime Springs, IA; 2008 (E19IA081275)	5	Soybean/ 5726085	Difenoconazole 250EC	0.2226	14	0.0217 0.152	ND ND	0.0590 0.0635	<0.01 <0.01
Lime Springs, IA; 2008 (E19IA081276)	5	Soybean/ 5726085	Difenoconazole 250EC	0.2188	14	0.0668 0.0920	<0.01 <0.01	0.0340 0.0295	<0.01 <0.01
Richland, IA; 2008 (C18IA081277)	5	Soybean/ Pioneer 93M11	Difenoconazole 250EC	0.2218	15	<0.01 <0.01	ND ND	0.0575 0.0462	<0.01 <0.01
Hedrick, IA; 2008 (C18IA081278)	5	Soybean/ 93M11	Difenoconazole 250EC	0.2200	14	<0.01 <0.01	ND <0.01	0.0555 0.0418	<0.01 <0.01
Gardner, ND; 2008 (C12MN081279)	5	Soybean/ 5B077RR	Difenoconazole 250EC	0.2237	14	0.0436 0.0230	<0.01 <0.01	0.274 0.272	0.0160 0.0200
Perley, MN; 2008 (C12MN081280)	5	Soybean/ 5A009RR	Difenoconazole 250EC	0.2237	14	<0.01 <0.01	ND ND	0.264 0.282	0.0134 0.0128

[1] End use product; 2.08 lb/gal EC formulation.
[2] The validated LOQ was 0.01 ppm. TA = triazole alanine. TAA = triazole acetic acid. T = 1,2,4-triazole. DALA = Days after last application. ND = Not detected.
[3] Samples were taken at additional sampling intervals for a residue decline study.

TABLE C.4. Summary of Residue Data from Crop Field Trials with Difenoconazole.

Commodity	Total Applic. Rate (lb ai/A)	DALA	Residue Levels (ppm)[1]						
			N	Min.	Max.	HAFT*	Median (STMdR)	Mean (STMR)	Std. Dev.
Difenoconazole									
Soybean forage	0.2146-0.2293	0	40	5.24	14.3	13.9	8.91	9.04	2.5
Soybean hay	0.2146-0.2293	0	40	8.64	51.8	43.4	22.8	23.6	10.8
Soybean seed	0.2175-0.2244	11-17	40	<0.01	0.152	0.0869	0.01	0.0215	0.0
T									
Soybean forage	0.2146-0.2293	0	40	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Soybean hay	0.2146-0.2293	0	40	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Soybean seed	0.2175-0.2244	11-17	40	<0.01	<0.01	<0.01	<0.01	<0.01	NA
TA									
Soybean forage	0.2146-0.2293	0	40	<0.01	0.0755	0.0715	0.0231	0.0257	0.0
Soybean hay	0.2146-0.2293	0	40	<0.01	0.158	0.128	0.0372	0.0443	0.0
Soybean seed	0.2175-0.2244	11-17	40	0.0295	0.282	0.273	0.0855	0.107	0.1
TAA									
Soybean forage	0.2146-0.2293	0	40	<0.01	0.013	0.0119	0.01	0.0101	0.0
Soybean hay	0.2146-0.2293	0	40	<0.01	0.0515	0.0490	0.0194	0.0230	0.0
Soybean seed	0.2175-0.2244	11-17	40	<0.01	0.020	0.018	0.01	0.011	0.0

* HAFT = Highest Average Field Trial. TA = triazole alanine. TAA = triazole acetic acid. T = 1,2,4-triazole. DALA = Days after last application.
[1] Mean, median, HAFT, and standard deviations were calculated by the reviewer. The LOQ (0.01 ppm for all analytes) was used for calculations for any results reported as <LOQ in Table C.3. Does not include additional sampling intervals collected for the residue decline study.

Figure C.1.1 Residue Decline of Difenoconazole in Soybean (Seven Springs, NC trial).

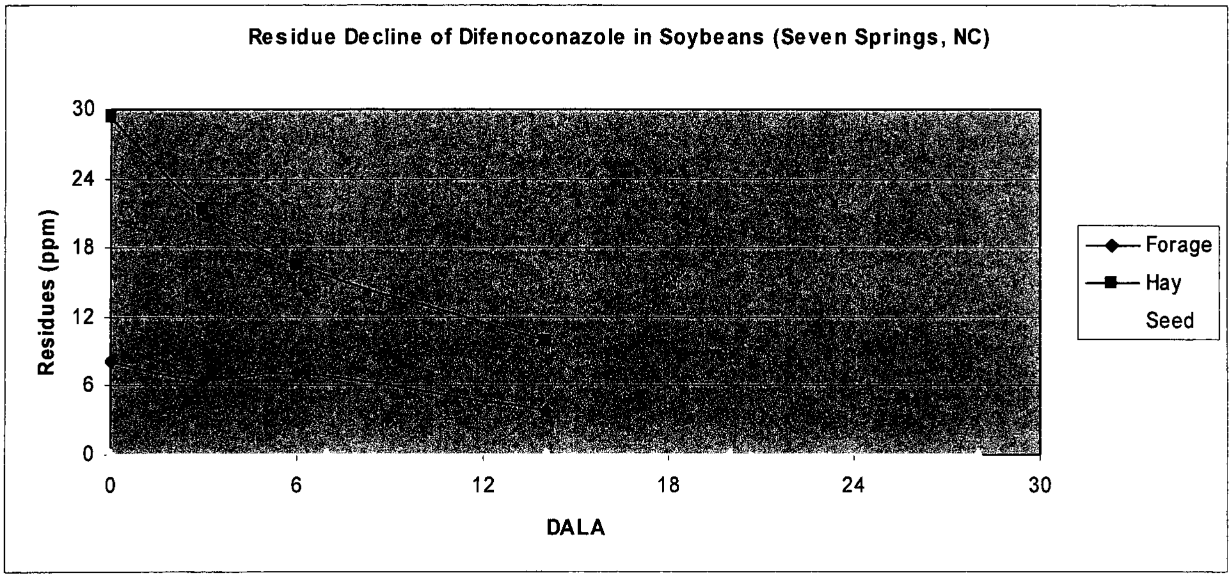
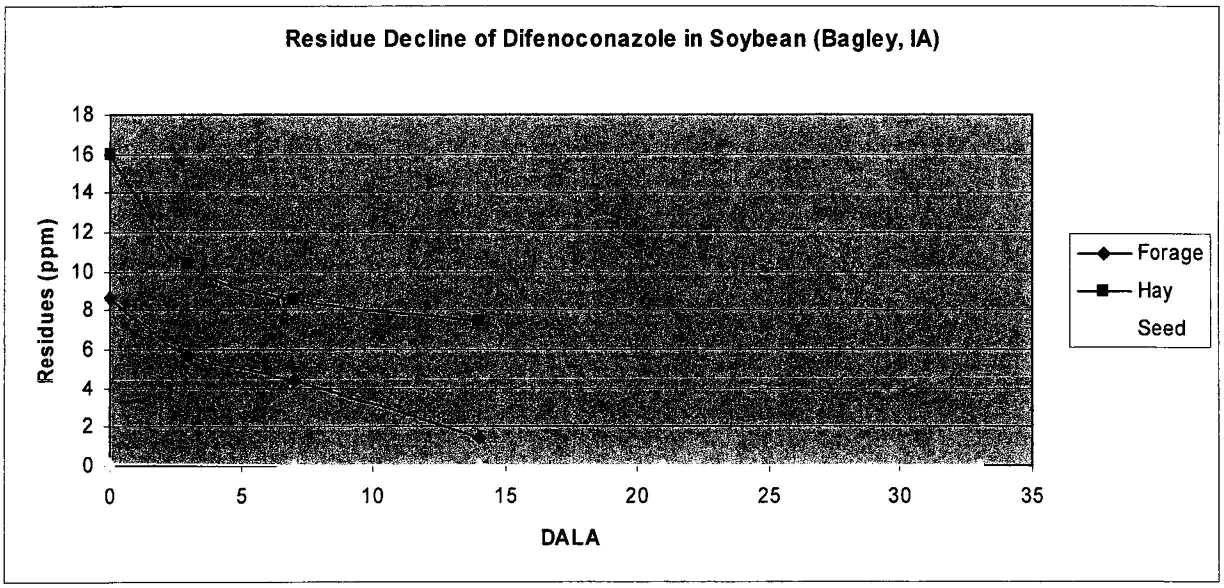


Figure C.1.2 Residue Decline of Difenoconazole in Soybean (Bagley, IA trial).



D. CONCLUSION

The field trial data reflect use of difenoconazole (EC formulation) as two foliar broadcast applications at a nominal rate of 0.11 lb ai/A per application for a total seasonal rate of 0.22 lb ai/A. The data reflect RTIs of 5-8 days and 0 days PHI for forage and hay and 11-17 days PHI for seed.

Acceptable methods were used for the determination of residues of difenoconazole and the triazole metabolites. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of soybean seed, forage, and hay samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted soybean field trial data.

There was no unusual weather conditions reported that may have adversely impacted the results of the study. Additionally, it does not appear that the agricultural practices used adversely impacted the results of the study.

E. REFERENCES

DP#: 172067 and 178394
Subject: PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS# 9029, 9895.
From: R. Lascola
To: J. Stone/C. Giles-Parker
Dated: 10/26/92
MRIDs: 42090001-42090004, 42090032-42090059, and 42303901

DP#: 340379
Subject: PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From: W. Wassell/M. Sahafeyan
To: D. Rosenblatt/S. Brothers
Dated: 8/9/07
MRIDs: 46950215-46950237

DP# 356135
Subject: Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From: B. Cropp-Kohlligian
To: J. Bazuin/T. Kish
Dated: 9/17/09
MRIDs: 47413501 and 47413502

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number(s): 9F7676
DP # 378829
PC Code: 128847

Template Version June 2005.

Primary Evaluator: Bonnie Cropp-Kohlligian, Environmental Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Bonnie Cropp-Kohlligian

Approved by: Susan V. Hummel, Chemist/Senior Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Susan V. Hummel

This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted (1/06/2011). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47929801. Willard, T.; Mayer, T. (2009) Difenoconazole - Magnitude of the Residues in or on Soybean: Final Report. Project Number: T002400-07, ML08-1488-SYN. Unpublished study prepared by Syngenta Crop Protection, Inc. 597 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection, Inc. submitted processing studies for difenoconazole on soybean. In three crop field trials conducted in ND, an emulsifiable concentrate (EC) formulation of difenoconazole was applied two times to soybean at an exaggerated rate (5x) of 0.55 lb ai/A, for a total nominal application rate of 1.1 lb ai/A (actual application rates of 1.09-1.12 lb ai/A). Two trials were conducted to produce processed fraction samples and one trial was conducted to produce aspirated grain fraction (AGF) samples. The re-treatment intervals were 7 days. Soybean seed was harvested at 12 to 15 day pre-harvest intervals (PHI) and processed into AGF, meal, hulls, and refined oil by GLP Technologies (Navasota, TX) using simulated commercial procedures. Adequate descriptions were provided of the processing procedures, including material balance summaries.

Samples of soybean seed, AGF, and processed commodities (meal, hull, and refined oil) were analyzed for residues of difenoconazole using modified method Syngenta REM 147.08, "Residue Method for the Determination of Residues of Difenoconazole (CGA-169374) in Various Crops and Processed Crop Fractions" using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Additionally, residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) were measured using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". The limit of quantitation (LOQ) was 0.01 ppm for each analyte in all matrices. The methods were adequate for data collection based on concurrent method recoveries.

The maximum storage duration of difenoconazole samples from harvest/processing to extraction for analysis was 146 days (4.8 months) for soybean seed (RAC), 98 days (3.2 months) for soybean meal, 167 days (5.5 months) for soybean hulls, 96 days (3.2 months) for refined oil, and 316 days (10.4 months) for AGF. The maximum storage duration of triazole metabolite samples from harvest/processing to extraction for analysis was 154 days (5.1 months) for soybean seed (RAC), 127 days (4.2 months) for soybean meal, 149 days (4.9 months) for soybean hulls, 124 days (4.1 months) for refined oil, and 306 days (10.1 months) for AGF. All samples were analyzed within 7 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year and in all processed commodities for at least two years, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of soybean seed, meal, hull, refined oil, and AGF samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted soybean processing data.

At the Northwood, ND site, in which samples were treated at a total rate 1.09 lb ai/A, residues of difenoconazole in/on soybean seed ranged <0.01-0.0247 ppm; average residues were <LOQ in meal, 0.0538 ppm in hulls, and 0.0169 ppm in refined oil. At the Gardner, ND site, in which samples were treated at a total rate of 1.12 lb ai/A, residues of difenoconazole in/on soybean seed ranged 0.0496-0.107 ppm; average residues were <LOQ in meal, 0.0464 ppm in hulls, and 0.0319 ppm in refined oil. The results of the study indicate that residues of difenoconazole concentrate in hulls (average processing factor of 2.0x) but do not concentrate in meal and refined oil (<1x).

At the Northwood, ND site, residues of TA were 0.113-0.164 ppm in/on soybean seed following treatment at a total rate 1.09 lb ai/A; average residues were 0.148 ppm in meal, 0.0507 ppm in hulls, and <LOQ in refined oil. At the Gardner, ND site, residues of TA were 0.555-0.605 ppm in/on soybean seed following treatment at a total rate 1.12 lb ai/A; average residues were 0.558 ppm in meal, 0.224 ppm in hulls, and <LOQ in refined oil. The results of the study indicate that residues of TA do not concentrate in meal, hulls, and refined oil (≤1x).

At the Northwood, ND site, residues of TAA were below the LOQ (<0.01 ppm) in/on all samples of soybean seed, meal, hulls, and refined oil following treatment at a total rate 1.09 lb ai/A. At the Gardner, ND site, residues of TAA were 0.0194-0.0216 ppm in/on soybean seed following treatment at a total rate 1.12 lb ai/A; average residues were 0.0328 ppm in meal, 0.0139 ppm in hulls, and <LOQ in refined oil. The results of the study indicate that residues of TAA concentrate slightly in meal (average processing factor of 1.3x) but do not concentrate in hulls and refined oil (<1x).

At both sites, residues of metabolite T were below the LOQ (<0.01 ppm) in/on all samples of soybean seed, meal, hulls, and refined oil. Therefore, no processing factors were calculated.

All of the processing factors calculated in this study were less than the maximum theoretical concentration factors of 11.3x for hulls, 2.2x for meal, and 12.0x for refined oil (based on separation of components; OPPTS 860.1520, Table 3).

Residue data from the soybean AGF study indicate that residues of difenoconazole were 0.310-0.368 ppm in/on soybean seed (RAC) and 190-244 ppm for AGF (resulting in a processing factor of 622x) following treatment at a total rate 1.12 lb ai/A. Residues of metabolite T were not detected above the LOQ (<0.01 ppm) for soybean seed. Residues of metabolite T were 0.0210-0.0255 ppm for AGF (resulting in a processing factor of 2.4x). Residues of metabolite TA were 0.590-0.615 ppm for soybean seed and 0.106-0.132 ppm for AGF (resulting in a processing factor of 0.2x) and residues of metabolite TAA were 0.0322-0.0350 ppm for soybean seed and 0.205-0.224 ppm for AGF (resulting in a processing factor of 6.4x).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# 378829].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: soil characterization, weather data, maintenance chemical applications, irrigation practices, field history records, tank mix storage stability data, and field samples weights were not collected under GLP. These deviations did not impact the validity of the study.

A. BACKGROUND INFORMATION

Difenoconazole is a broad-spectrum fungicide which belongs to the triazole (including the conazole) class of chemicals. It was developed under the code number CGA-169374.

The chemical structure and nomenclature of difenoconazole and the triazole metabolites are presented in Table A.1. The physicochemical properties of the technical grade of difenoconazole are presented in Table A.2.

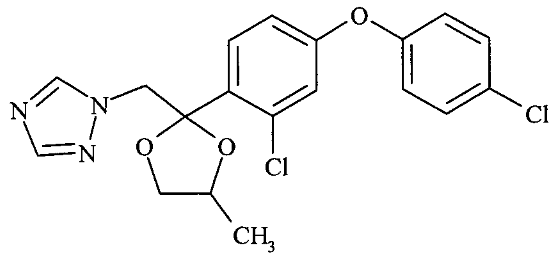
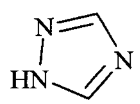
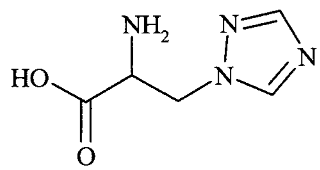
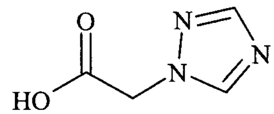
TABLE A.1. Test Compound Nomenclature.			
Compound			
Common name	Difenoconazole		
Company experimental name	CGA-169374		
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole		
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole		
CAS registry number	119446-68-3		
End-use product (EP)	Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole (Inspire®; EPA Reg. No. 100-1262)		
Compound			
Chemical name	Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

TABLE A.2. Physicochemical Properties of Difenoconazole.		
Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	
Solvent solubility	g/100 mL at 25 °C: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5 x 10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, $Log(K_{OW})$	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

B. EXPERIMENTAL DESIGN

Three field trials were conducted in ND. Two of the trials were conducted to produce processed commodity samples and one trial was conducted to produce aspirated grain fraction (AGF) samples. Test plots were treated with Difenoconazole 250EC, containing 2.08 lb/gal difenoconazole in an emulsifiable concentrate (EC) formulation. Soybeans were treated with two foliar broadcast applications at 5x the target application rate of 0.55 lb ai/A (total seasonal rate of 1.1 lb ai/A). Applications were made at re-treatment intervals of 7 days. The actual trial use patterns are reported in Table B.1.2.

B.1. Application and Crop Information

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants
		Method; Timing (Crop growth stage)	Volume[2] GPA	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Northwood, ND; 2008 (C13ND081270)	Difenoconazole 250EC	1. Post foliar broadcast; BBCH 82	29.97	0.5476	-	1.0898	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 88	29.67	0.5422	7		NIS at 0.125% v/v
Gardner, ND; 2008 (C12MN081279)	Difenoconazole 250EC	1. Post foliar broadcast; BBCH 85	20.09	0.5514	-	1.1174	NIS at 0.2% v/v
		2. Post foliar broadcast; 87	20.62	0.5660	7		NIS at 0.2% v/v
Gardner, ND; 2008 (C12ND081281)	Difenoconazole 250EC	1. Post foliar broadcast; BBCH 81	24.85	0.5695	-	1.1233	COC at 0.1% v/v
		2. Post foliar broadcast; BBCH 86	21.15	0.5538	7		COC at 0.1% v/v

NIS = Non-ionic surfactant. COC = Crop oil concentrate.
[1] EP = End-use Product; an emulsifiable concentrate (EC) difenoconazole formulation containing 2.08 lb ai/gal.
[2] GPA = gallons per acre.
[3] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Composite samples of soybean seed from the control and treated plots were collected and shipped frozen (processing trials) or ambient (AGF trial) to GLP Technologies (Navasota, TX) for processing into AGF, hulls, meal, and refined oil. After processing, samples were shipped on dry ice to Syngenta Crop Protection, Inc. (Greensboro, NC) for preparation. Samples of seed (RAC), hulls, meal, and aspirated grain fractions were ground in a table-top mill. Refined oil required no further preparation. After preparation, samples were shipped frozen to Morse Laboratories, LLC (Sacramento, CA) for analysis. At the analytical laboratory, samples were stored in temperature-monitored freezers at -20 ± 5 °C until analysis.

The processing procedure simulated commercial operations of soybean production as closely as possible to generate the required fraction of soybean seed (RAC), AGF, hulls, meal, and refined oil, with some variations to commercial methods. The processed fractions were stored frozen at <10 °F at the processing facility. Processing flowcharts for soybean AGF and processed meal, hulls, and refined oil fractions, copied without alteration from MRID 47929801, are presented below in Figures 1.1 (AGF) and 1.2 (meal, hulls, and refined oil).

FIGURE 1.1. Processing Flowchart for Soybean (AGF).

FORM H.217 Revision 00

MATERIAL BALANCE for GENERATION, CLASSIFICATION, AND ASH CONTENT DETERMINATION OF ASPIRATED GRAIN FRACTIONS

Sample # 1 (Control, Trt 1)   Code # 001

COMMODITY 1346.3 lbs.

Drying 1336.1 lbs. (after drying)

1336.1 lbs. used for generation

Aspiration 71.7 g

Classification

– ASPIRATED GRAIN FRACTION > 2360 micron 18.5 g

– ASPIRATED GRAIN FRACTION > 2000 micron 0.8 g

– ASPIRATED GRAIN FRACTION > 1180 micron 0.8 g

– ASPIRATED GRAIN FRACTION > 850 micron 0.4 g

– ASPIRATED GRAIN FRACTION > 425 micron 1.0 g

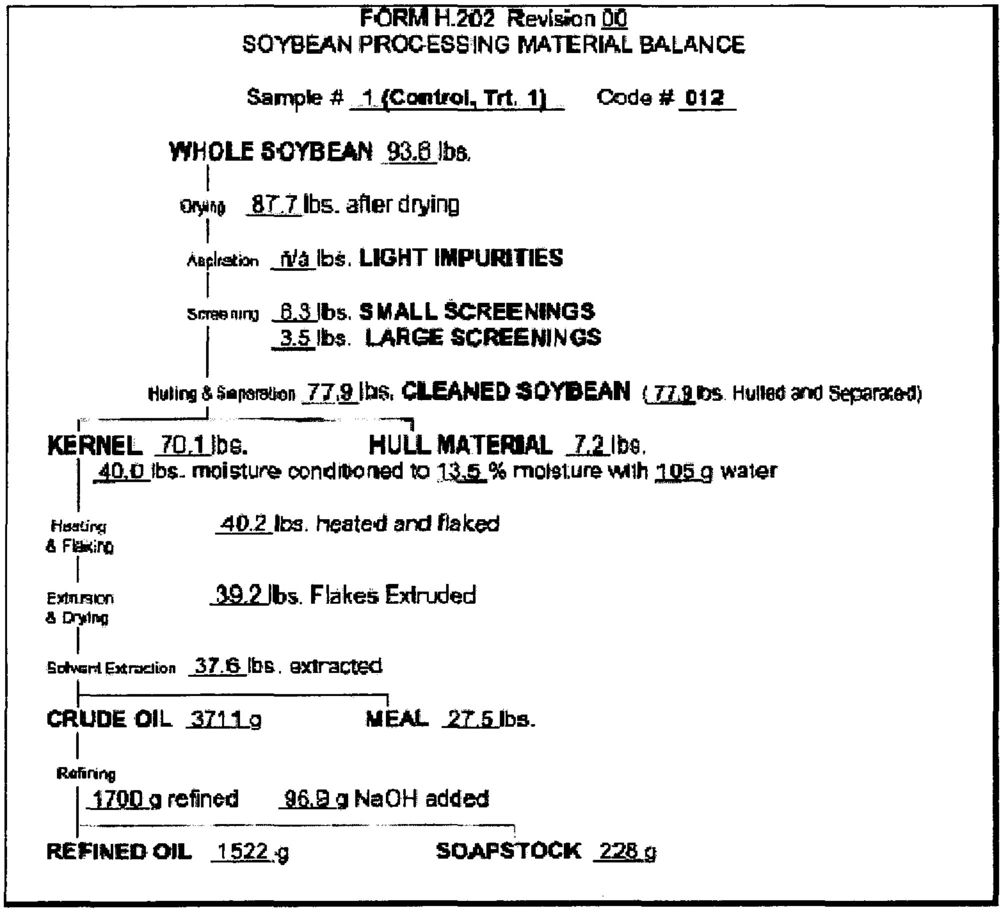
ASPIRATED GRAIN FRACTION < 425 micron 49.8 g

RECOMBINATION per Sponsor Instructions

0.7 g < 2360 micron and > 2000 micron
0.8 g > 1180 micron
0.3 g > 850 micron
0.0 g > 425 micron
49.8 g < 425 micron

ASH CONTENT 33.0 %

FIGURE 1.2. Processing Flowchart for Soybean (Meal, Hulls, Refined Oil).



FORM H.202 Revision 00
SOYBEAN PROCESSING MATERIAL BALANCE

Sample # 1 (Control, Trt. 1) Code # 012

WHOLE SOYBEAN 93.8 lbs.

Drying 87.7 lbs. after drying

Aspiration n/a lbs. LIGHT IMPURITIES

Screening 6.3 lbs. SMALL SCREENINGS
3.5 lbs. LARGE SCREENINGS

Hulling & Separation 77.9 lbs. CLEANED SOYBEAN (77.9 lbs. Hulled and Separated)

KERNEL 70.1 lbs. HULL MATERIAL 7.2 lbs.
40.0 lbs. moisture conditioned to 13.5 % moisture with 105 g water

Heating & Flaking 40.2 lbs. heated and flaked

Extrusion & Drying 39.2 lbs. Flakes Extruded

Solvent Extraction 37.6 lbs. extracted

CRUDE OIL 3711 g MEAL 27.5 lbs.

Refining
1700 g refined 96.9 g NaOH added

REFINED OIL 1522 g SOAPSTOCK 228 g

B.3. Analytical Methodology

Samples of soybean seed (RAC) and its processed fractions (AGF, meal, hulls, and refined oil) were analyzed for residues of difenoconazole with modified analytical method Syngenta REM 147.08 titled "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS". Soybean RAC and processed samples were analyzed for residues of difenoconazole triazole metabolites 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) with modified analytical method Morse Laboratories, Inc. Analytical Method No. 160 Revision 2 titled "Determination of 1,2,4-Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". Both methods have been reviewed previously by HED (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan). Brief descriptions of the methods were included in the submission.

Residues of difenoconazole in soybean samples were extracted by refluxing with methanol/concentrated ammonium hydroxide (80:20, v:v). Aliquots of the extracts were diluted with ultra-pure water, cleaned up using solid phase extraction, and analyzed using high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). Residues of metabolites T, TA, and TAA were extracted with methanol/water (80:20, v/v). Following the addition of Celite, the extracts were vacuum filtered, rinsed, and brought to volume with methanol/water (80:20, v:v). Aliquots of the TAA extract were purified by solid phase extraction and then derivatized by HCl/butanol esterification. The TA aliquot underwent two derivatizations: an esterification using HCL/butanol and an acylation using heptafluoro butyric anhydride (HFBA). The T aliquot was directly derivatized with dansyl chloride to produce the dansyl derivative of 1,2,4-triazole and partitioned into ethyl acetate. All metabolite extracts were then evaporated to dryness, redissolved in acetonitrile/water (30:70, v/v), and analyzed using HPLC with mass spectrometric (MS/MS) detection.

The LOQ was 0.01 ppm for difenoconazole in all soybean matrices; the corresponding LOD was 0.000125 ppm. The LOQ (as respective parent equivalents) was 0.01 ppm for the triazole metabolites T, TA, and TAA. The LOD was 0.00003 ppm for T and TA and 0.00005 ppm for TAA in all soybean matrices.

The methods were validated in conjunction with the analysis of processing samples. For concurrent recoveries of difenoconazole, control samples of seed (RAC) were fortified at 0.01, 0.10, 5.0, and 10 ppm, control samples of meal and hulls were fortified at 0.01 and 5.0 ppm, control samples of refined oil were fortified at 0.01 and 0.5 ppm, and control samples of AGF were fortified at 0.01, 0.05, 10, and 250 ppm. For concurrent recoveries of the triazole metabolite T, control samples of seed were fortified at 0.01, 0.1, and 0.5 ppm, control samples of meal, hulls, and refined oil were fortified at 0.01 and 0.1 ppm, and control samples of AGF were fortified at 0.01 and 0.5 ppm. For concurrent recoveries of the triazole metabolite TA, control samples of seed were fortified at 0.1, 0.25, 0.5, and 2.5 ppm, control samples of meal were fortified at 0.2 and 0.8 ppm, control samples of hulls were fortified at 0.1 and 0.8 ppm, control samples of refined oil were fortified at 0.01 and 0.1 ppm, and control samples of AGF were fortified at 0.04, 0.8, and 1.5 ppm. For concurrent recoveries of the triazole metabolite TAA, control samples of seed were fortified at 0.01, 0.10, and 0.5 ppm, control samples of meal, hulls, and refined oil were fortified at 0.01 and 0.1 ppm, and control samples of AGF were fortified at 0.02, 0.5, and 0.6 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are summarized in Table C.2. After processing, samples were stored frozen (-10 °C) until analysis. The maximum storage duration of difenoconazole samples from harvest/processing to extraction for analysis was 146 days (4.8 months) for soybean seed (RAC), 98 days (3.2 months) for soybean meal, 167 days (5.5 months) for soybean hulls, 96 days (3.2 months) for refined oil, and 316 days (10.4 months) for AGF. The maximum storage duration of metabolite samples from harvest/processing to extraction for analysis was 154 days (5.1 months) for soybean seed (RAC), 127 days (4.2 months) for soybean meal, 149 days (4.9 months) for soybean hulls, 124 days (4.1 months) for refined oil, and 306 days (10.1 months) for AGF. Analysis took place between 0 and 7 days after extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year and in all processed commodities for at least two years, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of soybean seed, meal, hull, refined oil, and AGF samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted soybean processing data.

Concurrent method recovery data are presented in Table C.1. The modified LC/MS-MS methods (Syngenta REM 147.08 and Morse Laboratories, Inc. Analytical Method No. 160 Revision 2) used for determining residues of difenoconazole and the triazole metabolites T, TA, and TAA in/on soybean RAC and processed fractions were adequately validated in conjunction with the analysis of field trial samples. Concurrent recoveries were within the acceptable range of 70-120% with one exception: at the 0.10 ppm spike level, recovery of 122% for T in seed. However, all mean recoveries were within the acceptable range.

Apparent residues of difenoconazole were <LOQ to 0.0544 ppm for seed (RAC) and 0.0181 ppm for AGF in/on control samples of soybeans. Apparent residues of difenoconazole were <LOQ in/on control samples of soybean meal, hulls, and refined oil samples. The mean residue levels for all metabolites found in the treated samples at the target application rate were similar to the levels found in the untreated samples. Apparent residues of TA in/on control samples of soybean were 0.0680 to 0.600 ppm for seed (RAC), 0.113 to 0.388 ppm for meal, 0.0259 to 0.182 ppm for hulls, and 0.342 ppm for AGF. Apparent residues of TA in/on control samples of refined oil were <LOQ. Apparent residues of TAA in/on control samples of soybean were <LOQ to 0.0272 ppm for seed (RAC), <LOQ to 0.0275 ppm for meal, <LOQ to 0.0135 ppm for hulls, and 0.0304 ppm for AGF. Apparent residues of TAA in/on control samples of soybean refined oil were all <LOQ. Apparent residues of T in/on control samples of soybean RAC and processed fractions were all <LOQ. The petitioner attributed the occurrence of residues of TA and TAA in/on untreated samples to the widespread use of triazoles and the non-specific nature of the common moiety method of analysis. Adequate example chromatograms were provided.

Residue data from the soybean processing study are reported in Table C.3. Residues of difenoconazole were <0.01-0.107 ppm for soybean seed (RAC), <0.01 ppm for meal, 0.0448-0.0540 ppm for hulls (resulting in processing factors of 0.6-3.4x; average 2.0x), and 0.0158-0.0355 ppm for refined oil (resulting in processing factors of 0.4-1.1x). Residues of metabolite T were each below the LOQ (<0.01 ppm for all analytes) in/on all samples of soybean seed, meal, hulls, and refined oil. Therefore, no processing factors were calculated. Residues of metabolite TA were 0.113-0.605 ppm for soybean seed (RAC), 0.143-0.570 ppm for meal (resulting in processing factors of 1.0x), 0.0493-0.226 ppm for hulls (resulting in processing factors of 0.3-

0.4x), and <0.01 ppm for refined oil. Residues of metabolite TAA were <0.01-0.0216 ppm for soybean seed (RAC), <0.01-0.0340 ppm for meal (resulting in a processing factor of 1.6x; average 1.3x), <0.01-0.0151 ppm for hulls (resulting in a processing factor of 0.7x), and <0.01 ppm for refined oil.

Residue data from the soybean AGF study are reported in Table C.3. Residues of difenoconazole were 0.310-0.368 ppm for soybean seed (RAC) and 190-244 ppm for AGF (resulting in processing a factor of 622x). Residues of metabolite T were not detected above the LOQ (<0.01 ppm) for soybean seed. Residues of metabolite T were 0.0210-0.0255 ppm for AGF (resulting in a processing factor of 2.4x). Residues of metabolite TA were 0.590-0.615 ppm for soybean seed and 0.106-0.132 ppm for AGF (resulting in a processing factor of 0.2x) and residues of metabolite TAA were 0.0322-0.0350 ppm for soybean seed and 0.205-0.224 ppm for AGF (resulting in a processing factor of 6.4x).

All of the processing factors calculated in this study were less than the maximum theoretical concentration factors of 11.3x for hulls, 2.2x for meal, and 12.0x for refined oil (based on separation of components; OPPTS 860.1520, Table 3).

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Soybean and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)[1]
Seed	Difenoconazole	0.01	11	101, 95, 94, 104, 70, 94, 106, 110, 100, 113, 93	98 ± 12
		0.10	9	98, 90, 102, 78, 98, 110, 117, 97, 99	99 ± 11
		5	1	108	NA
		10	1	116	NA
	1,2,4-Triazole	0.01	12	100, 79, 107, 89, 104, 93, 84, 80, 77, 95, 82, 77	89 ± 11
		0.10	10	96, 85, 122, 89, 77, 87, 84, 88, 96, 97	92 ± 12
		0.5	2	98, 99	99
	Triazole Acetic Acid	0.01	12	98, 101, 83, 86, 105, 104, 83, 101, 98, 105, 105, 96	97 ± 8
		0.10	10	99, 104, 93, 93, 88, 102, 107, 104, 106, 96	99 ± 6
		0.5	2	102, 107	105
	Triazole Alanine	0.10	10	86, 71, 103, 112, 84, 100, 77, 102, 80, 92	91 ± 13
		0.25	2	90, 83	87
		0.5	10	87, 78, 101, 97, 89, 89, 78, 102, 97, 94	91 ± 9
		2.5	2	84, 86	85
Meal	Difenoconazole	0.01	1	112	NA
		5.0	1	104	
	1,2,4-Triazole	0.01	1	82	
		0.1	1	83	

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Soybean and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)[1]
	Triazole Acetic Acid	0.01	1	90	NA
		0.1	1	97	
	Triazole Alanine	0.2	1	88	
		0.8	1	84	
Hulls	Difenoconazole	0.01	1	110	
		5.0	1	101	
	1,2,4-Triazole	0.01	1	92	
		0.1	1	93	
	Triazole Acetic Acid	0.01	1	83	
		0.1	1	98	
	Triazole Alanine	0.1	1	98	
		0.8	1	94	
Refined oil	Difenoconazole	0.01	1	86	
		0.5	1	90	
	1,2,4-Triazole	0.01	1	77	
		0.1	1	94	
	Triazole Acetic Acid	0.01	1	95	
		0.1	1	98	
	Triazole Alanine	0.01	1	106	
		0.1	1	102	
AGF	Difenoconazole	0.01	1	119	
		0.05	1	104	
		10.0	1	111	
		250	1	116	
	1,2,4-Triazole	0.01	2	80, 93	87
		0.5	2	91, 89	90
	Triazole Acetic Acid	0.02	1	98	NA
		0.5	2	99, 93	96
		0.6	1	98	NA
	Triazole Alanine	0.04	1	72	NA
		0.8	2	102, 77	90
		1.5	1	105	NA

[1] Standard deviations were calculated only for fortification levels having ≥3 samples.

TABLE C.2. Summary of Storage Conditions.

Matrix	Analyte	Storage Temperature (°C)	Actual Storage Duration[1]	Limit of Demonstrated Storage Stability[2]
Seed (RAC)	Difenoconazole	<-10	96-146 days (3.2-4.8 months)	None provided with the subject submission; however, based on previously submitted storage stability data (DP#s 340379 and 356135), when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable at -20°C for up to two years in/on cotton seed, cotton oil, and cotton meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw. Although the available storage stability data are not sufficiently representative for all processed commodities, which usually requires an oilseed, a fruit/fruiting vegetable, and a non-oily grain, when taken as a whole, the available data are deemed adequate to demonstrate the stability of residues of difenoconazole *per se* in all processed commodities for up to two years when stored under frozen conditions.
	Triazole metabolites (T, TA, TAA)		138-154 days (4.5-5.1 months)	
Meal	Difenoconazole		33-98 days (1.1-3.2 months)	
	Triazole metabolites (T, TA, TAA)		62-127 days (2.0-4.2 months)	
Hulls	Difenoconazole		99-167 days (3.3-5.5 months)	
	Triazole metabolites (T, TA, TAA)		81-149 days (2.7-4.9 months)	
Refined oil	Difenoconazole		32-96 days (1.1-3.2 months)	
	Triazole metabolites (T, TA, TAA)		60-124 days (2.0-4.1 months)	
AGF	Difenoconazole		316 days (10.4 months)	
	Triazole metabolites (T, TA, TAA)		306 days (10.1 months)	None provided with the subject study; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016).

[1] Interval from harvest/processing to extraction for analysis. Extracts were stored 0-7 days prior to analysis. Samples were stored 8 to 99 days before processing.

TABLE C.3. Residue Data from Soybean Processing Studies with Difenoconazole.

RAC	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Residues (ppm)				Processing Factor[2,3]			
				Difenoconazole	T	TA	TAA	Difenoconazole	T	TA	TAA
Northwood, ND; 2008 (C13ND081270)											
Soybean	Seed (RAC)	1.0898	15	0.0247 0.0128 <0.01 **(0.0158)**	ND ND ND	0.113 0.164 0.160 **(0.146)**	<0.01 <0.01 <0.01	--	--	--	--
	Meal			<0.01 <0.01 **(<0.01)**	ND <0.01	0.143 0.152 **(0.148)**	<0.01 <0.01	0.6x	NC	1.0x	NC
	Hulls			0.0540 0.0536 **(0.0538)**	ND ND	0.0520 0.0493 **(0.0507)**	<0.01 <0.01	3.4x	NC	0.3x	NC
	Refined oil			0.0158 0.0180 **(0.0169)**	ND ND	ND ND	ND ND	1.1x	NC	NC	NC
Gardner, ND; 2008 (C12MN081279)											
Soybean	Seed (RAC)	1.1174	14	0.0496 0.0744 0.107 **(0.0770)**	ND ND ND	0.555 0.585 0.605 **(0.582)**	0.0194 0.0199 0.0216 **(0.0203)**	--	--	--	--
	Meal			<0.01 <0.01 **(<0.01)**	<0.01 <0.01	0.545 0.570 **(0.558)**	0.0340 0.0315 **(0.0328)**	0.1x	NC	1.0x	1.6x
	Hulls			0.0448 0.0480 **(0.0464)**	<0.01 <0.01	0.221 0.226 **(0.224)**	0.0126 0.0151 **(0.0139)**	0.6x	NC	0.4x	0.7x
	Refined oil			0.0282 0.0355 **(0.0319)**	ND ND	ND ND	ND ND	0.4x	NC	NC	NC
Average[4]											
Soybean	Meal							<1x	NC	1.0x	1.3x
	Hulls							2.0x	NC	<1x	<1x
	Refined oil							<1x	NC	NC	NC
Gardner, ND; 2008 (C12ND081281)											
Soybean	Seed (RAC)	1.1233	12	0.363 0.310 0.368 **(0.347)**	ND <0.01 ND **(<0.01)**	0.615 0.605 0.590 **(0.603)**	0.0322 0.0350 0.0325 **(0.0332)**	--	--	--	--
	AGF (RAC)			190 214 244 **(216)**	0.0255 0.0210 0.0240 **(0.0235)**	0.132 0.106 0.113 **(0.117)**	0.214 0.205 0.224 **(0.214)**	622x	2.4x	0.2x	6.4x

1 Samples were analyzed in duplicate/triplicate; average residues are **bolded** and reported in parentheses.
2 NC = Not calculated; residues were below the LOQ (<0.01 ppm for all in analytes) in the processed fraction.
3 Processing Factor = [Measured residue for analyte in the processed fraction] / [Measured residue for analyte in the RAC].
4 In the calculation of the average processing factor, a value of 1.0 was used when a processing factor was not calculated due to residues <LOQ in the processed fraction.

D. CONCLUSION

The submitted soybean processing studies are acceptable. Processing of the seed RAC with quantifiable residues of difenoconazole resulted in the concentration of residues in certain soybean fractions but not in others (average processing factor provided in parenthesis). Residues of difenoconazole concentrate in AGF (622x) and hulls (2.0x) but do not concentrate in meal and refined oil (<1x). Residues of 1,2,4-T were below the LOQ in/on all samples of soybean seed, meal, hulls, and refined oil but did concentrate in AGF (2.4x). Residues of TA did not concentrate in soybean meal, hulls, refined oil, and AGF. Residues of TAA concentrate in AGF (6.4x) and meal (1.3x) but do not concentrate in hulls and refined oil (<1x).

Acceptable methods were used for the determination of residues of difenoconazole and the triazole metabolites. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year and in all processed commodities for at least two years, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of soybean seed, meal, hull, refined oil, and AGF samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted soybean processing data.

E. REFERENCES

DP#:	172067 and 178394
Subject:	PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS# 9029, 9895.
From:	R. Lascola
To:	J. Stone/C. Giles-Parker
Dated:	10/26/92
MRIDs:	42090001-42090004, 42090032-42090059, and 42303901

DP#:	340379
Subject:	PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From:	W. Wassell/M. Sahafeyan
To:	D. Rosenblatt/S. Brothers
Dated:	8/9/07
MRIDs:	46950215-46950237

DP#	356135
Subject:	Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	J. Bazuin/T. Kish
Dated:	9/17/09
MRIDs:	47413501 and 47413502

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number(s): 9F7676
DP # 378829
PC Code: 128847

Template Version June 2005

Primary Evaluator:	Bonnie Cropp-Kohlligian, Environmental Scientist Risk Assessment Branch 4 Health Effects Division (7509P) Bonnie Cropp-Kohlligian	Date: 2/23/2011
Approved by:	Susan V. Hummel, Chemist/Senior Scientist Risk Assessment Branch 4 Health Effects Division (7509P) Susan V. Hummel	Date: 2/23/2011

This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted (1/06/2011). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47929802. Hamilton, L. (2009) Difenoconazole – Magnitude of the Residue in or on Strawberries. Report No. T002401-07. Task No. T002401-07. Unpublished study prepared by Syngenta Crop Protection, Inc. 225 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole in/on strawberries. Nine trials were conducted in the United States during the 2007 and 2009 growing seasons, encompassing Zones 1 (NY; 1 trial), 2 (NC; 1 trial), 3 (FL; 1 trial), 5 (MN; 1 trial), 10 (CA; 4 trials), and 12 (WA; 1 trial). One treated plot and one untreated control plot were established at each trial site. The treated plots each received four foliar broadcast applications of an emulsifiable concentrate (EC) formulation containing 2.08 lb ai/gal (Difenoconazole 250 EC), at a nominal application rate of 0.115 lb ai/A. The total application rate was 0.45-0.47 lb ai/A. Applications were made 6-8 days apart using a backpack sprayer and a spray volume of 5.04 to 51.5 gal/A. One trial (Guadalupe, CA) was conducted at ~5 gal/A spray volume to simulate aerial application. NIS (Silwet, Kinetic or other nonionic surfactant) adjuvant was added to the spray mixtures at each test site. Strawberry fruit samples were collected 7 days after the third application and immediately following the fourth (last) application (PHI = 0). Samples were also collected at 1, 3 and 5 days after the last application (DALA) to generate residue decline data.

Residues of difenoconazole in strawberries were determined using Syngenta Analytical Method, REM 147.08, "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS", with some modifications. Residues of the triazole metabolites in strawberries were analyzed using Morse Labs Analytical Method No. Meth-160, Revision #2 (April 13, 2005), entitled "Determination of 1,2,4-Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices", with one modification. Residues of difenoconazole and the triazole metabolites were determined by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC/MS/MS). The limit of quantitation (LOQ) was determined to be 0.01 ppm, for both difenoconazole and the triazole metabolites. The limit of detection (LOD) was determined to be 0.00125 ng for difenoconazole and 0.0015 ng for the triazole metabolites.

All concurrent recovery values were within the acceptable range of 70-120%. Residues were detected with values <LOQ in several of the control samples. The petitioner corrected the concurrent recoveries for residues detected in the controls.

The maximum frozen storage interval from sampling to extraction was 255 days (8.2 months) for strawberries. Sample extracts were analyzed within 19 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs), when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of strawberry samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted strawberry field trial data.

Following four foliar applications of difenoconazole at a total rate of 0.46 lb ai/A, difenoconazole residues in/on strawberries harvested at a PHI of 0 days ranged from 0.0704 ppm to 1.22 ppm. Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of strawberry fruit; TA: <0.01-0.083 ppm in/on strawberry fruit; and TAA: <0.01-0.0123 ppm in/on strawberry fruit. Samples were also collected 7 days after the third application. For those samples, difenoconazole residues in/on strawberries harvested at a PHI of 7 days ranged from 0.0908 ppm to 0.590 ppm. Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of strawberry fruit; TA: <0.01-0.0875 ppm in/on strawberry fruit; and TAA: <0.01-0.0257 ppm in/on strawberry fruit.

At the Santa Maria, CA test site (Trial No. W30CA078485), additional samples were collected at 1, 3, and 5 days after the last treatment to determine the decline of difenoconazole. Residues of difenoconazole *per se* in/on strawberry (fruit) were relatively stable from the 0 DALA to 5 DALA sampling intervals.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, DP# 378829.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The study described was conducted to meet the requirements of EPA Good Laboratory Practice Standards (40 CFR Part 160) with the following exceptions:

1. Weather data were not collected according to the FIFRA-GLP requirements; NOAA weather data are reported. These data are ancillary and do not affect the integrity of the study;
2. Spray mix storage stability data were not generated as required in 40 CFR 160.113(a)(3);
3. Maintenance chemicals and irrigation were not applied under GLP;
4. Soil characterization was not conducted under GLP.

These reported deviations from regulatory requirements did not have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Difenoconazole is a broad-spectrum fungicide which belongs to the triazole (including the conazole) class of chemicals. It was developed under the code number CGA-169374.

The chemical structure and nomenclature of difenoconazole and the triazole metabolites are presented in Table A.1. The physicochemical properties of the technical grade of difenoconazole are presented in Table A.2.

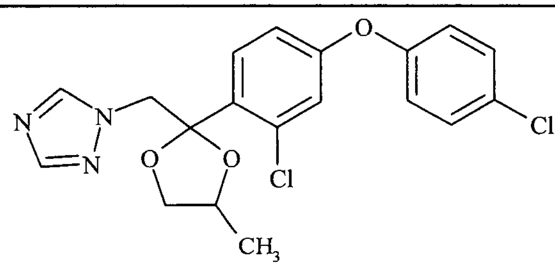
TABLE A.1. Test Compound Nomenclature.	
Compound	
Common name	Difenoconazole
Company experimental name	CGA-169374
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CAS registry number	119446-68-3
End-use product (EP)	Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole (Inspire®; EPA Reg. No. 100-1262)

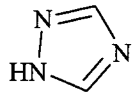
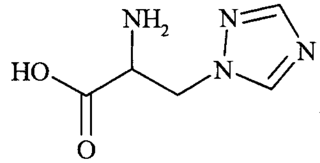
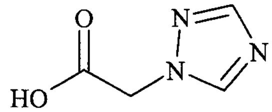
TABLE A.1. Test Compound Nomenclature.			
Compound			
Chemical name	Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

TABLE A.2. Physicochemical Properties of Difenoconazole.		
Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	
Solvent solubility	g/100 mL at 25 °C: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5 x 10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, $Log(K_{OW})$	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Refer to Table B.1.1 for trial site conditions, Table B.1.2 for study use patterns, and Table B.1.3 for trial numbers and geographical locations.

TABLE B.1.1 Trial Site Conditions.				
Trial Identification: City, State; Year (Trial No.)	Soil characteristics			
	Type	% OM	pH	CEC (meq/100 g)
Penn Yan, NY; 2007 (Trial No. E03NY078481)	Sandy Loam	2.6	6.4	12.2
Seven Springs, NC; 2007 (Trial No. E10NC078482)	Sand	0.7	6.8	3.4
Wimauma, FL; 2007 (Trial No. E16FL078483)	Sand	1.2	6.2	2.8

TABLE B.1.1 Trial Site Conditions.				
Trial Identification: City, State; Year (Trial No.)	Soil characteristics			
	Type	% OM	pH	CEC (meq/100 g)
Fertile, MN; 2007 (Trial No. C12MN078484)	Sandy Loam	4.0	7.8	13.5
Santa Maria, CA; 2007 (Trial No. W30CA078485)	Loamy Sand	0.58	7.2	8.2
Madera, CA; 2007 (Trial, No. W29CA078486)	Sandy Loam	1.1	7.7	9.6
Madera, CA; 2007 (Trial No. W29CA078487)	Loamy Sand	0.5	8.2	6.9
Mount Vernon, WA; 2007 (Trial No. W19WA078488)	Silt Loam	3.5	6.2	13.9
Guadalupe, CA; 2009 (Trial No. W33CA098489)	Sand	0.5	7.5	8.1

The actual temperature recordings were within average 10 year historical values for the residue study period. The actual rainfall average was also generally within the 10-year historical rainfall average. Irrigation was used to supplement rainfall, as needed. A history of maintenance chemicals used just prior to and during the test was provided. A two-year maintenance chemical history was not provided.

TABLE B.1.2. Study Use Pattern.								
Location City, State; Year (Trial No.)	EP [1]	Application						Tank Mix/ Adjuvants[4]
		Method	Timing	Volume [2] GPA	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Penn Yan, NY; 2007 (Trial No. E03NY078481)	Difenoconazole 250 EC	Post Foliar Broadcast Application	BBCH 65	29.78	0.117	--	0.46	NIS at 0.127-0.133% v/v
			BBCH 73	30.41	0.117	6		
			BBCH 81	29.73	0.115	8		
			BBCH 89	29.98	0.115	7		
Seven Springs, NC; 2007 (Trial No. E10NC078482)	Difenoconazole 250 EC	Post Foliar Broadcast Application	BBCH 81	25.59	0.115	--	0.46	NIS at 0.0124-0.125% v/v
			BBCH 81	25.40	0.115	7		
			BBCH 83	23.89	0.111	7		
			BBCH 85	25.18	0.116	7		
Wimauma, FL; 2007 (Trial No. E16FL078483)	Difenoconazole 250 EC	Post Foliar Broadcast Application	Ripe Berries	51.50	0.118	--	0.46	NIS at 0.125% v/v
			Green, Ripe Fruit and Flowers	49.11	0.113	7		
			Ripe Berries	50.41	0.116	7		
			Ripe Fruit	48.72	0.112	7		
Fertile, MN; 2007 (Trial No. C12MN078484)	Difenoconazole 250 EC	Post Foliar Broadcast Application	BBCH 63	12.10	0.118	--	0.47	NIS at 0.125-0.134% v/v
			BBCH 65	18.03	0.116	8		
			BBCH 73	14.99	0.115	6		

TABLE B.1.2. Study Use Pattern.

Location City, State; Year (Trial No.)	EP [1]	Application						Tank Mix/ Adjuvants[4]
		Method	Timing	Volume [2] GPA	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
			BBCH 88	15.90	0.123	7		
Santa Maria, CA; 2007 (Trial No. W30CA078485)	Difenoconazole 250 EC	Post Foliar Broadcast Application	BBCH 89	30.18	0.116	--	0.46	NIS at 0.124% v/v
			BBCH 89	30.10	0.116	7		
			BBCH 89	29.94	0.115	7		
			BBCH 89	29.91	0.115	7		
Madera, CA; 2007 (Trial No. 29CA078486)	Difenoconazole 250 EC	Post Foliar Broadcast Application	BBCH 71	20.02	0.116	--	0.47	NIS at 0.124% v/v
			BBCH 75	20.13	0.117	7		
			BBCH 79	19.91	0.115	8		
			BBCH 79	20.18	0.117	7		
Madera, CA; 2007 (Trial No. W29CA078487)	Difenoconazole 250 EC	Post Foliar Broadcast Application	BBCH 73	20.06	0.116	--	0.47	NIS at 0.124% v/v
			BBCH 77	20.13	0.117	7		
			BBCH 79	20.03	0.116	7		
			BBCH 79	20.19	0.117	7		
Mount Vernon, WA; 2007 (Trial No. W19WA078488)	Difenoconazole 250 EC	Post Foliar Broadcast Application	Green Fruit/Bloom	26.51	0.111	--	0.45	NIS at 0.125-0.127% v/v
			Green Fruit	26.96	0.110	7		
			Mature Fruit	28.94	0.117	7		
			Ripe Fruit	29.59	0.114	7		
Guadalupe, CA; 2009 (Trial No. W33CA098489)	Difenoconazole 250 EC	Post Foliar Broadcast Application	BBCH 75	5.06	0.117	--	0.47	NIS at 0.120% v/v
			BBCH 75	5.06	0.117	7		
			BBCH 75	5.04	0.116	7		
			BBCH 75	5.05	0.117	7		

[1] EP = End-use Product; Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole
[2] GPA = Gallons per acre
[3] Retreatment Interval.
[4] NIS = Silwet or Kinetic or other nonionic surfactant

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions[1]	Strawberry		
	Submitted	Requested	
		Canada	U.S.
1	1	NA	1
2	1	NA	1
3	1	NA	1
4		NA	
5	1	NA	1
6		NA	
7		NA	
8		NA	
9		NA	
10	4[2]	NA	3
11		NA	
12	1	NA	1
13		NA	
Total	9		8

[1] Regions 14-21 and 1A, 5A, 5B, and 7A were not included as the proposed use is for the US only.
[2] Field trial W33CA098489 (Guadalupe, CA) was added to the protocol in June 2009 to ensure that application was made at a low volume (5 GPA) to simulate aerial application.
NA = not applicable.

B.2. Sample Handling and Preparation

Strawberry fruit samples were collected 7 days after the third application and immediately following the fourth (last) application. Two replicate samples were obtained by collecting mature fruit from at least 12 separate areas of the plot with a minimum weight of approximately 3 lbs. Samples were also collected at 1, 3 and 5 days after the last application to generate a residue decline curve. A single treated sample was collected for each decline interval. A single replicate of the untreated control was collected for each treatment at all designated sampling intervals.

After collection, all samples were frozen and shipped via freezer truck or overnight courier with dry ice to the Syngenta Greensboro, NC facility, except field trial W33CA098489. Upon arrival, samples were stored frozen until prepared for analysis. Freezers were maintained at approximately -20 °C with continuous temperature monitoring. Samples from trial W33CA098489 were shipped directly to Morse Laboratories, LLC in Sacramento, CA where they were stored frozen until prepared for analysis.

Inedible portions of the commodity were removed and any adhering soil was removed by lightly brushing. Strawberries were composited and ground in a Hobart food cutter. Dry ice was used as necessary to keep the sample frozen. After preparation, samples were stored in polyethylene bags or bottles labeled with field test number, project number, sample code number, and crop identification and were maintained frozen until analyzed.

B.3. Analytical Methodology

Samples of strawberry were analyzed for residues of difenoconazole with modified analytical method Syngenta REM 147.08 titled "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS". Additionally, strawberry samples were analyzed for residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". Both methods have been reviewed previously by HED (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan). Brief descriptions of the methods were included in the submission.

Residues of difenoconazole in strawberry samples were extracted by refluxing with methanol/concentrated ammonium hydroxide (80:20, v:v). Aliquots of the extracts were diluted with ultra-pure water, cleaned up using solid phase extraction, and analyzed using high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). Residues of metabolites T, TA, and TAA were extracted with methanol/water (80:20, v/v). Following the addition of Celite, the extracts were vacuum filtered, rinsed, and brought to volume with methanol/water (80:20, v:v). Aliquots of the TAA extract were purified by solid phase extraction and then derivatized by HCl/butanol esterification. The TA aliquot underwent two derivatizations: an esterification using HCL/butanol and an acylation using heptafluorobutyric anhydride (HFBA). The T aliquot was directly derivatized with dansyl chloride to produce the dansyl derivative of 1,2,4-triazole and partitioned into ethyl acetate. All metabolite extracts were then evaporated to dryness, redissolved in acetonitrile/water (30:70, v/v), and analyzed using HPLC with mass spectrometric (MS/MS) detection.

The LOQ was determined to be 0.01 ppm, for both difenoconazole and the triazole metabolites. The limit of detection (LOD) was determined to be 0.00125 ng for difenoconazole and 0.0015 ng for the triazole metabolites.

The methods were validated in conjunction with the analysis of field trial samples. For concurrent recoveries of difenoconazole, control samples of strawberry were fortified at 0.01, 0.50, 1.0, and 2.0 ppm. For concurrent recoveries of the triazole metabolites T and TAA, control samples of strawberry were fortified at 0.01, 0.10, and 0.50 ppm. For concurrent recoveries of the triazole metabolite TA, control samples of strawberry were fortified at 0.01, 0.02, 0.20, and 0.50 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. The maximum storage interval from sampling to extraction was 255 days (8.2 months) for strawberries. Sample extracts were analyzed within 19 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs), when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of strawberry samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted strawberry field trial data.

Concurrent method recovery data are presented in Table C.1. The modified LC/MS-MS methods (Syngenta REM 147.08 and Morse Laboratories, Inc. Analytical Method No. 160 Revision 2) used for determining residues of difenoconazole and the triazole metabolites T, TA, and TAA in/on strawberry were adequately validated in conjunction with the analysis of field trial samples. Concurrent recoveries ranged from 70% to 119% for difenoconazole fortifications, ranged from 71% to 107% for 1,2,4-triazole (T) fortifications, ranged from 77% to 104% for triazole alanine (TA) fortifications, and ranged from 93% to 118% for triazole acetic acid (TAA) fortifications. All recoveries were within the acceptable range of 70-120%.

Apparent residues of difenoconazole, 1,2,4-T, and TAA were below the LOQ (<0.01 ppm) in/on all samples of untreated strawberry. Apparent residues of TA were below the LOQ (<0.01 ppm) in/on samples of untreated strawberry (n = 11). Quantifiable apparent residues of TA were observed in/on 10 samples of untreated strawberry fruit (0.0134-0.0342 ppm). The petitioner attributed the occurrence of residues of TA in/on untreated samples to the widespread use of triazoles and the non-specific nature of the common moiety method of analysis. Adequate example chromatograms were provided.

Residue data from the field trials are reported in Table C.3. A summary of the residue data is presented in Table C.4.

Following four foliar applications of difenoconazole at a total rate of 0.46 lb ai/A, difenoconazole residues in/on strawberries harvested at a PHI of 0 days ranged from 0.0704 ppm to 1.22 ppm. Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of strawberry fruit; TA: <0.01-0.083 ppm in/on strawberry fruit; and TAA: <0.01-0.0123 ppm in/on strawberry fruit. Samples were also collected 7 days after the third application. For those samples, difenoconazole residues in/on strawberries harvested at a PHI of 7 days ranged from 0.0908 ppm to 0.590 ppm. Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of strawberry fruit; TA: <0.01-0.0875 ppm in/on strawberry fruit; and TAA: <0.01-0.0257 ppm in/on strawberry fruit.

At the Santa Maria, CA test site (Trial No. W30CA078485), additional samples were collected at 1, 3, and 5 days after the last treatment to determine the decline of difenoconazole (Figure C.1). Residues of difenoconazole *per se* in/on strawberry (fruit) were relatively stable from the 0 DALA to 5 DALA sampling intervals.

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and Triazole Metabolites.

Matrix	Analyte	Fortification Level (ppm)	Recovery (%)[1]	Average Recovery per Fortification Level (%)	Standard Deviation[2]	n
Strawberries	Difenoconazole	0.01	105, 107, 101, 96, 70, 89, 94, 109,	96.4	12.8	8
		0.50	119, 103, 108, 71, 99, 92	98.5	16.3	6
		1.00	114, 91	102.6	NA	2
		2.00	97	NA	NA	1
Strawberries	1,2,4-Triazole (T)	0.01	71, 84, 107, 91, 77, 88, 85, 80, 90	86	10.2	9
		0.10	84, 85, 93, 99, 85, 90, 87	89	5.3	7
		0.50	91, 91	91	NA	2
Strawberries	Triazole Alanine (TA)	0.01	93, 94, 81, 83, 104	91	9.2	5
		0.02	77, 104, 100, 84	91	12.8	4
		0.20	90, 94, 97, 94	94	3.1	4
		0.50	96, 96, 95, 88, 98	95	4.0	5
Strawberries	Triazole Acetic Acid (TAA)	0.01	97, 100, 94, 95, 110, 109, 118, 100, 107	103	8.1	9
		0.10	99, 101, 104, 103, 102, 105, 104	103	2.0	7
		0.50	93, 107	100	NA	2

1 The recovery values were corrected for residues detected in the controls by the study author.
2 Standard deviations were only calculated for sample size ≥3.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Maximum Storage Interval[1]	Interval of Demonstrated Storage Stability
Strawberries	-20 ± 5	255 days (8.2 months)	None provided with the subject submission; however, based on previously submitted storage stability data (DP#s 340379 and 356135), when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable at -20°C for up to two years in/on cotton seed, cotton oil, and cotton meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw. None provided with the subject study; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016).

1 Actual storage duration from sampling to extraction. All samples were analyzed within 19 days of extraction.

TABLE C.3. Residue Data from Strawberry Field Trials with Difenoconazole.

City, State, Region;Year (Trial Identification No.)	Crop; Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days) [1]	Residues (ppm)[2]			
					Difenoconazole	1,2,4-Triazole	Triazole Alanine	Triazole Acetic Acid
Penn Yan, NY, Region 1; 2007 (Trial No. E03NY078481)	Strawberry; Honeoye	Mature Fruit	0.345	7	0.307	ND	0.0214	<0.01
			0.345	7	0.247	<0.01	0.0202	<0.01
			0.46	0	0.638	ND	0.0284	<0.01
			0.46	0	0.658	<0.01	0.0285	<0.01
Seven Springs, NC, Region 2; 2007 (Trial No. E10NC078482)	Strawberry; Camarosa	Mature Fruit	0.345	7	0.198	<0.01	0.0162	<0.01
			0.345	7	0.189	<0.01	0.0156	<0.01
			0.46	0	0.378	<0.01, ND[3], ND[3]	0.358[4], 0.0148[3], 0.0136[3]	<0.01, <0.01[3], <0.01[3]
			0.46	0	0.432	<0.01, ND[3], ND[3]	0.0154, 0.0174[3], 0.0128[3]	<0.01, <0.01[3], <0.01[3]
Wimauma, FL, Region 3; 2007 (Trial No. E16FL078483)	Strawberry; Treasures	Mature Fruit	0.345	7	0.129	ND	0.0540	<0.01
			0.345	7	0.178	ND	0.0500	<0.01
			0.46	0	0.192	ND	0.0442	<0.01
			0.46	0	0.193	ND	0.0452	<0.01
Fertile, MN, Region 5; 2007 (Trial No. C12MN078484)	Strawberry; Mesabi	Mature Fruit	0.345	7	0.141	ND	0.0136	<0.01
			0.345	7	0.202	<0.01	0.0111	<0.01
			0.47	0	0.485	ND	<0.01	<0.01
			0.47	0	0.362	ND	<0.01	<0.01
Santa Maria, CA, Region 10; 2007 (Trial No. 30CA078485)	Strawberry; Albion	Mature Fruit	0.345	7	0.215	ND	0.0730	0.0128
			0.345	7	0.238	ND	0.0690	0.0117
			0.46	0	0.412	<0.01	0.0795	0.0123
			0.46	0	0.554	ND	0.0655	0.0117
			0.46	1	0.630	ND	0.0685	0.0120
			0.46	3	0.470	<0.01	0.0850	0.0154
			0.46	5	0.422	ND	0.0860	0.0157
Madera, CA, Region 10; 2007 (Trial No. 29CA078486)	Strawberry; Seascape	Mature Fruit	0.345	7	0.261	ND	0.0362	<0.01
			0.345	7	0.314	ND	0.0347	<0.01
			0.47	0	0.718	<0.01	0.0236	<0.01
			0.47	0	0.582	<0.01	0.0402	<0.01

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TABLE C.3. Residue Data from Strawberry Field Trials with Difenoconazole.

City, State, Region;Year (Trial Identification No.)	Crop; Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days) [1]	Residues (ppm)[2]			
					Difenoconazole	1,2,4-Triazole	Triazole Alanine	Triazole Acetic Acid
Madera, CA, Region 10; 2007 (Trial No. 29CA078487)	Strawberry; Chandler	Mature Fruit	0.345	7	0.539	ND	0.0417	<0.01
			0.345	7	0.590	ND	0.0466	<0.01
			0.47	0	1.20	<0.01	0.0640	<0.01
			0.47	0	1.22	<0.01	0.0346	<0.01
Mount Vernon, WA, Region 12; 2007 (Trial No. 19WA078488)	Strawberry; Puget Reiiance	Mature Fruit	0.345	7	0.129	ND	<0.01	<0.01
			0.345	7	0.0908	ND	<0.01	<0.01
			0.45	0	0.0736	ND	<0.01	<0.01
			0.45	0	0.0704	ND	<0.01	<0.01
Guadalupe, CA, Region 10; 2009 (Trial No. W33CA098489)	Strawberry; Albion	Mature Fruit	0.345	7	0.234	ND	0.0875	0.0238
			0.345	7	0.254	<0.01	0.0805	0.0257
			0.47	0	0.352	<0.01	0.0695	0.0238
			0.47	0	0.392	<0.01	0.0825	0.0234

1 Samples were collected at two intervals, seven days after the 3rd application and immediately following the 4th and final application.
2 The validated LOQ = 0.01 ppm for difenoconazole and triazole metabolites. ND = Not detected.
3 Confirmatory analysis. Average of triplicate analyses used in calculations in Table C.4.
4 Triazole alanine (TA) analysis outlier not used in calculations.

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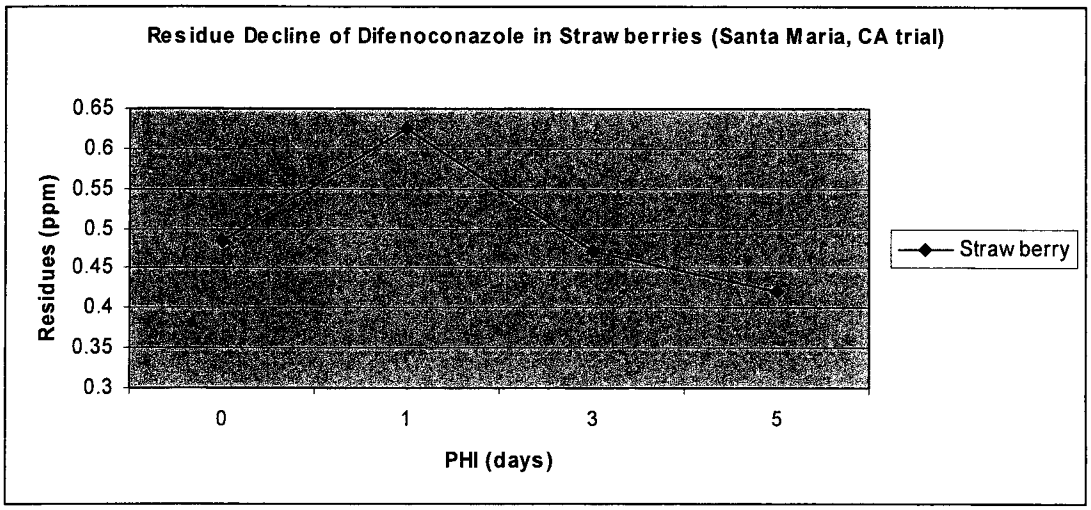
TABLE C.4. Summary of Residue Data from Crop Field Trials with Difenoconazole

Commodity	Total Application Rate (lb ai/A)	PHI (days)[1]	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
Difenoconazole									
Strawberries	0.35	7	18	0.0908	0.590	0.565	0.225	0.248	0.130
	0.46	0	18	0.0704	1.22	1.21	0.422	0.495	0.320
1,2,4-Triazole (T)									
Strawberries	0.35	7	18	<0.01	<0.01	<0.01	<0.01	<0.01	NA
	0.46	0	18	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Triazole Alanine (TA)									
Strawberries	0.35	7	18	<0.01	0.0875	0.084	0.035	0.038	0.026
	0.46	0	18	<0.01	0.083	0.0760	0.032	0.038	0.025
Triazole Acetic Acid (TAA)									
Strawberries	0.35	7	18	<0.01	0.0257	0.0248	0.01	0.012	0.005
	0.46	0	18	<0.01	0.0123	0.0120	0.01	0.01	0.000

[1] Samples were collected at two intervals, seven days after the 3rd application and immediately following the 4th and final application.
[2] HAFT = Highest Average Field Trial

Figure C.1 Residue Decline of Difenoconazole in Strawberry (Santa Maria, CA trial).



D. CONCLUSION

The field trial data reflect the use of difenoconazole (EC formulation) as three or four foliar broadcast applications at a nominal rate of 0.115 lb ai/A per application for a total seasonal rate of 0.345 lb ai/A (three applications) or 0.46 lb ai/A (four applications). The data reflect RTIs of 6-8 days. Strawberry samples were collected 7 days after the third application and immediately following the fourth (last) application. Difenoconazole decline samples collected at one test site 1, 3, and 5 days after the last application, showed little decline in residue levels of difenoconazole *per se* over the sampling interval.

Acceptable methods were used for the determination of residues of difenoconazole and the triazole metabolites. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs), when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of strawberry samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted strawberry field trial data.

There was no unusual weather conditions reported that may have adversely impacted the results of the study. Additionally, it does not appear that the agricultural practices used adversely impacted the results of the study.

E. REFERENCES

DP#:	172067 and 178394
Subject:	PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS# 9029, 9895.
From:	R. Lascola
To:	J. Stone/C. Giles-Parker
Dated:	10/26/92
MRIDs:	42090001-42090004, 42090032-42090059, and 42303901

DP#:	340379
Subject:	PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From:	W. Wassell/M. Sahafeyan
To:	D. Rosenblatt/S. Brothers
Dated:	8/9/07
MRIDs:	46950215-46950237

DP#	356135
Subject:	Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	J. Bazuin/T. Kish
Dated:	9/17/09
MRIDs:	47413501 and 47413502

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.

From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number(s): 9F7676
DP # 378829
PC Code: 128847

Template Version June 2005.

Primary Evaluator: Bonnie Cropp-Kohlligian, Environmental Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Bonnie Cropp-Kohlligian

Approved by: Susan V. Hummel, Chemist/Senior Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Susan V. Hummel

This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted (1/06/2011). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47929803. Willard, T.; Mayer, T. (2009) Difenoconazole - Magnitude of the Residues in or on Sweet or Tart Cherry, Peach, and Plum as Representative Commodities of Fruit, Stone, Group 12: Final Report. Project Number: T002402-07, ML08-1479-SYN. Unpublished study prepared by Syngenta Crop Protection, Inc. 413 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole on stone fruit (Crop Group 12) following four applications of an emulsifiable concentrate (EC) formulation containing 2.08 lb ai/gal (Difenoconazole 250 EC). Twenty-one stone fruit field trials were conducted in the United States and Canada during the 2008-2009 growing seasons. Six cherry trials (2 tart cherry; 4 sweet cherry) were conducted in Zones 1 (PA; 1 trial), 5 (MI; 1 trial), 10 (CA; 2 trials), and 11 (WA; 2 trials); nine peach trials were conducted in Zones 1 (NY; 1 trial), 2 (GA and NC; 3 trials), 5 (Ontario, Canada; 1 trial), 6 (TX; 1 trial), and 10 (CA; 3 trials); and six plum trials were conducted in Zones 5 (MI; 1 trial), 10 (CA; 4 trials), and 12 (OR; 1 trial).

Each field trial included one control plot and one treated plot in which the difenoconazole EC formulation was applied to stone fruit. Each plot was treated four times as a foliar broadcast application at a target rate of 0.115 lb ai/A (0.129 kg ai/ha), for a total seasonal nominal rate of 0.46 lb ai/A (0.52 kg ai/ha). Actual total application rates ranged from 0.46-0.47 lb ai/A (0.52-0.53 kg ai/ha) in the sweet cherry plots, 0.46-0.47 lb ai/A (0.51-0.52 kg ai/ha) in the tart cherry plots, 0.46-0.49 lb ai/A (0.51-0.55 kg ai/ha) in the peach plots, and 0.46-0.46 lb ai/A (0.51-0.52 kg ai/ha) in the plum plots. Re-treatment intervals ranged from 5 to 8 days. Crop oil concentrate, non-ionic surfactant, or miscible oil was added to all spray mixtures. Both dilute and concentrated spray volumes were represented in the cherry, peach, and plum field trials. Single control and duplicate treated samples of stone fruit (sweet cherry, tart cherry, peach, or plum) were harvested from each plot on the day of the last application (0 DALA).

Stone fruit samples were analyzed for residues of difenoconazole using modified method Syngenta REM 147.08, "Residue Method for the Determination of Residues of Difenoconazole (CGA-169374) in Various Crops and Processed Crop Fractions" using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Additionally, residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) were measured using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". The limit of quantitation (LOQ) was 0.01 ppm for each analyte in all matrices. The methods were adequate for data collection based on concurrent method recoveries.

The maximum storage duration from harvest to extraction for difenoconazole was 442 days (14.5 months) for tart cherry, 441 days (14.5 months) for sweet cherry, 157 days (5.2 months) for peach, and 427 days (14.0 months) for plum. The maximum storage duration from harvest to extraction for the triazole metabolites was 456 days (15.0 months) for tart cherry, 209 days (6.9 months) for sweet cherry, 401 days (13.2 months) for peach, and 148 days (4.9 months) for plum. All samples were analyzed within 42 days of extraction; all samples analyzed for residues of difenoconazole *per se* were analyzed within 8 days of extraction. The maximum storage duration from sampling to analysis was 381 days (12.5 months) for difenoconazole analysis and 356 days (11.7 months) for triazole metabolite analysis. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of peach samples from the subject submission. Available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on tomato are deemed adequate to support the storage intervals and conditions of cherry and plum samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted stone fruit field trial data.

Following four broadcast treatment applications of difenoconazole at a total rate of 0.4557-0.4713 lb ai/A, difenoconazole residues were 0.284-0.716 ppm in/on sweet cherry (0 DALA), 0.728-1.01 ppm in/on tart cherry (0 DALA), 0.073-1.02 ppm in/on peach (0 DALA), and 0.070-0.600 ppm in/on plum (0 DALA). Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of sweet cherry, tart cherry, peach, and plum; TA: 0.021-0.106 ppm in/on sweet cherry, 0.236-1.42 ppm in/on tart cherry, <0.01-0.825 ppm in/on peach, and 0.019-0.337 ppm in/on plum; and TAA: <0.01 ppm in/on sweet cherry, 0.011-0.096 ppm in/on tart cherry, <0.01-0.055 ppm in/on peach, and <0.01-0.011 ppm in/on plum.

At two trial sites (Fresno and Hughson, CA), samples of sweet cherry or peaches were taken at 0, 1, and 3 DALA to assess residue decline. At both trial sites, residues of difenoconazole *per se* in/on sweet cherries and peaches declined only slightly from the 0-day to 3-day sampling intervals.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# 378829].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: soil characterization, weather data, maintenance chemical applications, irrigation practices, field history records, tank mix storage stability data, and field samples weights were not collected under GLP. These deviations did not impact the validity of the study.

A. BACKGROUND INFORMATION

Difenoconazole is a broad-spectrum fungicide which belongs to the triazole (including the conazole) class of chemicals. It was developed under the code number CGA-169374.

The chemical structure and nomenclature of difenoconazole and the triazole metabolites are presented in Table A.1. The physicochemical properties of the technical grade of difenoconazole are presented in Table A.2.

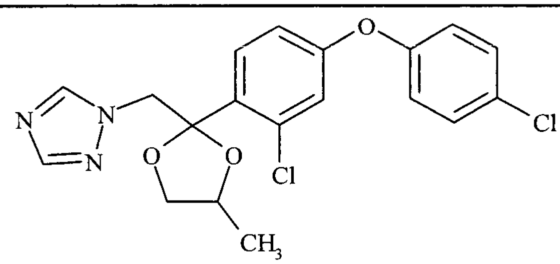
TABLE A.1. Test Compound Nomenclature.	
Compound	
Common name	Difenoconazole
Company experimental name	CGA-169374
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CAS registry number	119446-68-3

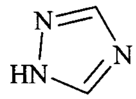
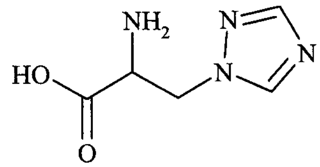
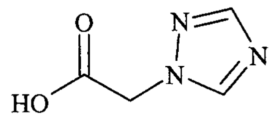
TABLE A.1. Test Compound Nomenclature.			
End-use product (EP)	Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole (Inspire®; EPA Reg. No. 100-1262)		
Compound			
Chemical name	Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

TABLE A.2. Physicochemical Properties of Difenoconazole.		
Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	
Solvent solubility	<u>g/100 mL at 25 °C</u>: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5 x 10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, Log(K_{OW})	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

B. EXPERIMENTAL DESIGN

Twenty-one stone fruit field trials were conducted in the United States and Canada during the 2008-2009 growing seasons. Six cherry trials (2 tart cherry; 4 sweet cherry) were conducted in Zones 1 (PA; 1 trial), 5 (MI; 1 trial), 10 (CA; 2 trials), and 11 (WA; 2 trials); nine peach trials were conducted in Zones 1 (NY; 1 trial), 2 (GA and NC; 3 trials), 5 (Ontario, Canada; 1 trial), 6 (TX; 1 trial), and 10 (CA; 3 trials); and six plum trials were conducted in Zones 5 (MI; 1 trial), 10 (CA; 4 trials), and 12 (OR; 1 trial). The plots received four foliar broadcast applications, at 5 to 8 day retreatment intervals, of the 250EC formulation of difenoconazole. Each application was made at a rate of 0.1129-0.1433 lb ai/A (0.127-0.161 kg ai/ha) for a total seasonal application rate of 0.4557-0.4869 lb ai/A (0.5108-0.5458 kg ai/ha). Applications were made using backpack, tractor, or airblast sprayers and a spray volume of ~10 to 212 gal/A (94-1,986 l/ha), with a non-ionic surfactant, crop oil concentrate, or miscible oil added to the spray mixture for all applications.

B.1. Study Site Information

TABLE B.1.1. Trial Site Conditions.

Trial Identification: City, State/Province; Year (Trial No.)	Soil characteristics			
	Type	%OM	pH	CEC meq/100 g
Cherry Trials				
Orefield, PA; 2008 (E04PA081151)	Loam	2.8	5.9	10.7
Hart, MI; 2008 (C01MI081172)	Sandy loam	2.6	6.9	6.7
Fresno, CA; 2008 (W29CA081153)	Loamy sand	0.4	6.6	4.4
Kerman, CA; 2008 (W30CA081154)	Loamy sand	0.86	7.5	3.6
Ephrata, WA; 2008 (W18WA081155)	Sandy loam	1.3	6.2	12.6
Ephrata, WA; 2008 (W18WA081156)	Sandy loam	1.3	6.8	11.5
Peach Trials				
Alton, NY; 2009 (E031175NY08)	Loam	2.0	6.8	11.4
Alto, GA; 2009 (E121176GA08)	Sandy clay loam	3.0	6.6	11.4
Pikeville, NC; 2009 (E101177NC08)	Sand	2.1	6.1	4.3
Athens, GA; 2008 (E12GA081160)	Clay loam	1.2	5.8	8.1
Branchton, Ontario, Canada; 2008 (C32CAN081173)	Loam	1.8	7.2	11.4
D'Hanis, TX; 2008 (W07TX081162)	Clay loam	2.4	8.1	28.6
Hughson, CA; 2008 (W26CA081163)	Loamy sand	0.8	7.5	7.4
Madera, CA; 2008 (W30CA081164)	Sandy loam	0.74	6.8	7.0
Kingsburg, CA; 2008 (W23CA081165)	Sandy loam	1.8	7.6	10.7
Plum Trials				
Hart, MI; 2008 (C01MI081174)	Sandy loam	2.6	6.9	6.7
Hughson, CA; 2008 (W26CA081167)	Sandy loam	0.4	4.8	9.3
Fresno, CA; 2008 (E19CA081168)	Sandy loam	1.73	7.3	5.3
Kerman, CA; 2008 (W29CA081169)	Sandy loam	1.2	6.8	9.4
Lindsay, CA; 2008 (W32CA081170)	Loam	1.2	7.4	17.0
Forest Grove, OR; 2008 (W19WA081171)	Silt loam	5.1	5.2	16.8

Maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. The crop varieties grown are identified in

Table C.3. Precipitation (total inches) and temperature data (overall range) during the study period were reported for each trial site. Comparisons to historical weather data were within normal ranges and no unusual weather conditions were noted.

TABLE B.1.2. Study Use Pattern.

Location (City, State/Province; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants[5]
		Method; Timing (Crop growth stage)[2]	Volume gal/A (l/ha)[3]	Rate lb ai/A (kg ai/ha)	RTI[4] (days)	Total Rate lb ai/A (kg ai/ha)	
Cherry Trials							
Orefield, PA; 2008 (E04PA081151)	Difenoconazole 250 EC	1. Post foliar broadcast; Straw color, first fruit coloring	79.17 (740.56)	0.1136 (0.127)	-	0.4557 (0.5108)	Miscible oil at 0.125% v/v
		2. Post foliar broadcast; Beginning of fruit coloring	79.33 (742.05)	0.1138 (0.128)	6		
		3. Post foliar broadcast; 85	78.75 (736.63)	0.1130 (0.127)	7		
		4. Post foliar broadcast; 87	80.40 (752.06)	0.1153 (0.129)	7		
Hart, MI; 2008 (C01MI081172)	Difenoconazole 250 EC	1. Post foliar broadcast; 73	127.64 (1193.94)	0.1170 (0.131)	-	0.4675 (0.5241)	NIS at 1% v/v
		2. Post foliar broadcast; 79-81	128.14 (1198.62)	0.1168 (0.131)	8		
		3. Post foliar broadcast; 88	128.72 (1204.05)	0.1169 (0.131)	7		
		4. Post foliar broadcast; 89	127.84 (1195.82)	0.1168 (0.131)	7		
Fresno, CA; 2008 (W29CA081153)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 71	174.94 (1636.39)	0.1163 (0.130)	-	0.4713 (0.5283)	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 71	174.31 (1630.50)	0.1174 (0.132)	6		
		3. Post foliar broadcast; BBCH 73	176.17 (1647.89)	0.1186 (0.133)	6		
		4. Post foliar broadcast; BBCH 77	176.74 (1653.23)	0.1190 (0.133)	8		
Kerman, CA; 2008 (W30CA081154)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 79	76.44 (715.02)	0.1165 (0.131)	-	0.4619 (0.5178)	COC at 0.5% v/v
		2. Post foliar broadcast; BBCH 81	76.42 (714.83)	0.1165 (0.131)	7		
		3. Post foliar broadcast; BBCH 81	75.66 (707.72)	0.1154 (0.129)	7		
		4. Post foliar broadcast; BBCH 87	74.46 (696.50)	0.1135 (0.127)	7		

TABLE B.1.2. Study Use Pattern.

Location (City, State/Province; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants[5]
		Method; Timing (Crop growth stage)[2]	Volume gal/A (l/ha)[3]	Rate lb ai/A (kg ai/ha)	RTI[4] (days)	Total Rate lb ai/A (kg ai/ha)	
Ephrata, WA; 2008 (W18WA081155)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 75	10.09 (94.38)	0.1164 (0.130)	-	0.4650 (0.5213)	COC at 0.127% v/v
		2. Post broadcast spray; Post foliar broadcast; BBCH 81	10.14 (94.85)	0.117 (0.131)	7		
		3. Post broadcast spray; Post foliar broadcast; BBCH 88	10.13 (94.76)	0.1147 (0.129)	7		
		4. Post broadcast spray; Post foliar broadcast; BBCH 89	10.33 (96.63)	0.1169 (0.131)	7		
Ephrata, WA; 2008 (W18WA081156)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 75	199.47 (1865.84)	0.1151 (0.129)	-	0.4612 (0.5170)	COC at 0.127% v/v
		2. Post foliar broadcast; BBCH 81	200.16 (1872.30)	0.1155 (0.129)	7		
		3. Post foliar broadcast; BBCH 88	200.10 (1871.74)	0.1155 (0.129)	7		
		Post foliar broadcast; BBCH 89	199.39 (1865.09)	0.1151 (0.129)	7		
Peach Trials							
Alton, NY; 2009 (E031175NY08)	Difenoconazole 250 EC	1. Post foliar broadcast; No. 76, Fruit ~60% final size	99.63 (931.94)	0.1150 (0.129)	-	0.4613 (0.5171)	NIS at 0.125% v/v
		2. Post foliar broadcast; No. 78, Fruit ~80% final size	99.89 (934.37)	0.1153 (0.129)	7		
		3. Post foliar broadcast; Beginning of fruit color	99.24 (928.29)	0.1145 (0.128)	7		
		4. Post foliar broadcast; Fruit ripe for picking	100.92 (944.01)	0.1165 (0.131)	7		
Alto, GA; 2009 (E121176GA08)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 77	211.39 (1977.34)	0.1155 (0.129)	-	0.4605 (0.5162)	COC at 0.125% v/v
		2. Post foliar broadcast; BBCH 78	209.20 (1956.86)	0.1143 (0.128)	7		
		3. Post foliar broadcast; BBCH 79-81	212.27 (1985.57)	0.1146 (0.128)	7		
		4. Post foliar broadcast; BBCH 81-83	210.79 (1971.73)	0.1161 (0.130)	7		

TABLE B.1.2. Study Use Pattern.

Location (City, State/Province; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants[5]
		Method; Timing (Crop growth stage)[2]	Volume gal/A (l/ha)[3]	Rate lb ai/A (kg ai/ha)	RTI[4] (days)	Total Rate lb ai/A (kg ai/ha)	
Pikeville, NC; 2009 (E101177NC08)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 75	83.47 (780.78)	0.1149 (0.129)	-	0.4612 (0.5170)	NIS at 0.328% v/v
		2. Post foliar broadcast; BBCH 78	80.64 (754.31)	0.1155 (0.129)	5		NIS at 0.341% v/v
		3. Post foliar broadcast; BBCH 85	85.19 (796.87)	0.1161 (0.130)	8		NIS at 0.325% v/v
		4. Post foliar broadcast; BBCH 89	84.47 (790.13)	0.1147 (0.129)	6		NIS at 0.323% v/v
Athens, GA; 2008 (E12GA081160)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 76-77	143.41 (1341.46)	0.1160 (0.130)	-	0.4641 (0.5203)	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 77	142.99 (1337.53)	0.1151 (0.129)	7		
		3. Post foliar broadcast; BBCH 79-80	141.74 (1325.84)	0.1157 (0.130)	7		
		4. Post foliar broadcast; BBCH 81-83	144.34 (1350.16)	0.1173 (0.131)	8		
Branchton, Ontario, Canada; 2008 (C32CAN081173)	Difenoconazole 250 EC	1. Post foliar broadcast; 76 to 77	85.20 (796.96)	0.1155 (0.129)	-	0.4616 (0.5175)	NIS at 0.125% v/v
		2. Post foliar broadcast; 77 to 78	88.23 (825.30)	0.1196 (0.134)	7		
		3. Post foliar broadcast; 79 to 81	83.84 (784.24)	0.1136 (0.127)	7		
		4. Post foliar broadcast; 85 to 87	83.34 (779.56)	0.1129 (0.127)	7		
D'Hanis, TX; 2008 (W07TX081162)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 79	122.40 (1144.93)	0.1139 (0.128)	-	0.4568 (0.5121)	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 75	153.08 (1431.91)	0.1130 (0.127)	7		
		3. Post foliar broadcast; BBCH 81	155.90 (1458.29)	0.1143 (0.128)	7		
		4. Post foliar broadcast; BBCH 85	161.63 (1511.89)	0.1156 (0.130)	7		

TABLE B.1.2. Study Use Pattern.

Location (City, State/Province; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants[5]
		Method; Timing (Crop growth stage)[2]	Volume gal/A (l/ha)[3]	Rate lb ai/A (kg ai/ha)	RTI[4] (days)	Total Rate lb ai/A (kg ai/ha)	
Hughson, CA; 2008 (W26CA081163)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 85, final size reached	154.30 (1443.32)	0.1161 (0.130)	-	0.4632 (0.5192)	NIS at 0.1% v/v
		2. Post foliar broadcast; BBCH 88, fruit beginning to soften	146.34 (1368.86)	0.1159 (0.130)	7		
		3. Post foliar broadcast; BBCH 88, fruit softening	145.62 (1362.13)	0.1154 (0.129)	7		
		4. Post foliar broadcast; BBCH 89, fully ripe	146.11 (1366.71)	0.1158 (0.130)	7		
Madera, CA; 2008 (W30CA081164)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 75	10.04 (93.91)	0.1150 (0.129)	-	0.4597 (0.5153)	COC at 0.5% v/v
		2. Post foliar broadcast; BBCH 81	10.06 (94.10)	0.1152 (0.129)	7		
		3. Post foliar broadcast; BBCH 85	10.04 (93.91)	0.1150 (0.129)	7		
		4. Post foliar broadcast; BBCH 87	10.00 (93.54)	0.1145 (0.128)	7		
Kingsburg, CA; 2008 (W23CA081165)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 85	67.97 (635.79)	0.1433 (0.161)	-	0.4869 (0.5458)	NIS at 0.5% v/v
		2. Post foliar broadcast; BBCH 85	96.87 (906.12)	0.1156 (0.130)	8		
		3. Post foliar broadcast; BBCH 85	91.77 (858.42)	0.1129 (0.127)	6		
		4. Post foliar broadcast; BBCH 89	84.65 (791.82)	0.1151 (0.129)	7		
Plum Trials							
Hart, MI; 2008 (C01MI081174)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 85	80.54 (753.37)	0.1137 (0.127)	-	0.4568 (0.5121)	NIS at 0.125% v/v
		2. Post foliar broadcast; BBCH 85-86	80.71 (754.96)	0.1140 (0.128)	8		
		3. Post foliar broadcast; BBCH 88	80.47 (752.72)	0.1151 (0.129)	6		
		4. Post foliar broadcast; BBCH 89	81.36 (761.04)	0.1140 (0.128)	7		

TABLE B.1.2. Study Use Pattern.

Location (City, State/Province; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants[5]
		Method; Timing (Crop growth stage)[2]	Volume gal/A (l/ha)[3]	Rate lb ai/A (kg ai/ha)	RTI[4] (days)	Total Rate lb ai/A (kg ai/ha)	
Hughson, CA; 2008 (W26CA081167)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 81, beginning of ripening	171.21 (1601.50)	0.1169 (0.131)	-	0.4638 (0.5199)	COC at 0.375% v/v
		2. Post foliar broadcast; BBCH 88, fruit beginning to soften	158.17 (1479.52)	0.1147 (0.129)	8		
		3. Post foliar broadcast; BBCH 88, fruit beginning to soften	160.26 (1499.07)	0.1162 (0.130)	7		
		4. Post foliar broadcast; BBCH 89, fully ripe	159.96 (1496.27)	0.1160 (0.130)	7		
Fresno, CA; 2008 (E19CA081168)	Difenoconazole 250 EC	1. Post foliar broadcast; 83	75.11 (702.58)	0.1149 (0.129)	-	0.4582 (0.5136)	NIS at 0.25% v/v
		2. Post foliar broadcast; 86	74.77 (699.40)	0.1144 (0.128)	7		
		3. Post foliar broadcast; 87	75.19 (703.33)	0.1150 (0.129)	7		
		4. Post foliar broadcast; 88	80.80 (755.80)	0.1139 (0.128)	7		
Kerman, CA; 2008 (W29CA081169)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 79	174.30 (1630.40)	0.116 (0.127)	-	0.4614 (0.5172)	NIS at 0.15% v/v
		2. Post foliar broadcast; BBCH 87	172.57 (1614.22)	0.1150 (0.129)	7		
		3. Post foliar broadcast; BBCH 88	172.42 (1612.82)	0.1150 (0.129)	7		
		4. Post foliar broadcast; BBCH 89	173.38 (1621.80)	0.1154 (0.129)	7		
Lindsay, CA; 2008 (W32CA081170)	Difenoconazole 250 EC	1. Post foliar broadcast; BBCH 81	94.04 (879.65)	0.1154 (0.129)	-	0.4591 (0.5147)	NIS at 0.5% v/v
		2. Post foliar broadcast; 85	94.38 (882.83)	0.1139 (0.128)	7		
		3. Post foliar broadcast; BBCH 87	54.31 (508.02)	0.1150 (0.129)	7		
		4. Post foliar broadcast; BBCH 89	59.84 (559.74)	0.1148 (0.129)	7		

TABLE B.1.2. Study Use Pattern.

Location (City, State/Province; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants[5]
		Method; Timing (Crop growth stage)[2]	Volume gal/A (l/ha)[3]	Rate lb ai/A (kg ai/ha)	RTI[4] (days)	Total Rate lb ai/A (kg ai/ha)	
Forest Grove, OR; 2008 (W19WA081171)	Difenoconazole 250 EC	1. Post foliar broadcast; immature fruit	101.28 (947.37)	0.1152 (0.129)	-	0.4603 (0.5160)	NIS at 0.15% v/v
		2. Post foliar broadcast; immature fruit	102.79 (961.50)	0.1169 (0.131)	6		
		3. Post foliar broadcast; immature fruit	110.94 (1037.73)	0.1139 (0.128)	7		
		4. Post foliar broadcast; mature fruit	111.40 (1042.04)	0.1143 (0.128)	7		

[1] EP = End-use Product; Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole.
[2] Difenoconazole was applied to the test plots 21 days, 14 days, 7 days, and on the day of harvest for applications 1, 2, 3, and 4, respectively.
[3] Gallons per acre; liters per hectare.
[4] Retreatment Interval.
[5] NIS = Non-ionic surfactant (Induce, Latron B-1956, Activator 90, Agral 90, Break Thru, K-90, or Activate Plus at 0.1-1.0% v/v). COC = Crop oil concentrate (Dyne-Amic, McGreggor Crop Oil M, or Helena Crop Oil Concentrate at 0.125-0.5% v/v). For the PA trial, miscible oil (Damoil, Drexel Chemical) was used rather than COC or NIS.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Tart Cherry[1]			Sweet Cherry[1]			Peach			Plum		
	Submitted	Requested[2]		Submitted	Requested[2]		Submitted	Requested[2]		Submitted	Requested[2]	
		Canada	U.S.		Canada	U.S.		Canada	U.S.		Canada	U.S.
1	1	NA	1	--	NA	--	1	NA	1	--	NA	--
1A	--	NA	--	--	NA	--	--	NA	--	--	NA	--
2	--	NA	--	--	NA	--	3	NA	3	--	NA	--
3	--	NA	--	--	NA	--	--	NA	--	--	NA	--
4	--	NA	--	--	NA	--	--	NA	--	--	NA	--
5	1	NA	4	--	NA	2	1	NA	1	1	NA	1
5A	--	NA	--	--	NA	--	--	NA	--	--	NA	--
5B	--	NA	--	--	NA	--	--	NA	--	--	NA	--
6	--	NA	--	--	NA	--	1	NA	1	--	NA	--
7	--	NA	--	--	NA	--	--	NA	--	--	NA	--
7A	--	NA	--	--	NA	--	--	NA	--	--	NA	--
8	--	NA	--	--	NA	--	--	NA	--	--	NA	--
9	--	NA	1	--	NA	--	--	NA	--	--	NA	--
10	--	NA	--	2	NA	2	3	NA	3	4	NA	4
11	--	NA	--	2	NA	2	--	NA	--	--	NA	--
12	--	NA	--	--	NA	--	--	NA	--	1	NA	1
13	--	NA	--	--	NA	--	--	NA	--	--	NA	--
14	--	NA	--	--	NA	--	--	NA	--	--	NA	--
15	--	NA	--	--	NA	--	--	NA	--	--	NA	--
16	--	NA	--	--	NA	--	--	NA	--	--	NA	--
17	--	NA	--	--	NA	--	--	NA	--	--	NA	--
18	--	NA	--	--	NA	--	--	NA	--	--	NA	--
19	--	NA	--	--	NA	--	--	NA	--	--	NA	--
20	--	NA	--	--	NA	--	--	NA	--	--	NA	--
21	--	NA	--	--	NA	--	--	NA	--	--	NA	--
Total	2	[illegible]	6	4	[illegible]	6	9	[illegible]	9	6	[illegible]	6

[1] A total of 6 cherry trials (sweet or tart cherry) is required for the stone fruit crop group (Table 2, OPPTS 860.1500).
[2] A 25% reduction was applied to the required number of trials, as the petitioner is requesting a tolerance for the stone fruit crop group.

B.2. Sample Handling and Preparation

At each trial, a single control and duplicate treated stone fruit samples (consisting of approximately 3 pounds for cherries and 24 fruit, ≥5 pounds for peaches and plums) were harvested on the day of the last application (DALA) of difenoconazole. At one cherry and one peach trial site (CA), additional single samples of stone fruit were taken at 1 and 3 DALA to assess residue decline.

Samples were shipped frozen to the preparation facility (Syngenta Crop Protection; Greensboro, NC), where they were stored at <-10 °C until sample preparation. The fruit were cut with a meat cleaver or knife and the stem and stone (pit) were removed and discarded. The composited samples were ground with dry ice in a Hobart foodcutter. The prepared samples were shipped frozen to Morse Laboratories (Sacramento, CA) and stored frozen at -20 ± 5 °C in temperature monitored freezers prior to analysis.

B.3. Analytical Methodology

Stone fruit samples were analyzed for residues of difenoconazole with modified analytical method Syngenta REM 147.08 titled "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS". Additionally, stone fruit samples were analyzed for residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". Both methods have been reviewed previously by HED (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan). Brief descriptions of the methods were included in the submission.

Residues of difenoconazole in stone fruit samples were extracted by refluxing with methanol/concentrated ammonium hydroxide (80:20, v:v). Aliquots of the extracts were diluted with ultra-pure water and cleaned up using solid phase extraction, and analyzed using high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). Residues of metabolites T, TA, and TAA were extracted with methanol/water (80:20, v/v). Following the addition of Celite, the extracts were vacuum filtered, rinsed, and brought to volume with methanol/water (80:20, v:v). Aliquots of the TAA extract were purified by solid phase extraction and then derivatized by HCl/butanol esterification. The TA aliquot underwent two derivatizations: an esterification using HCL/butanol and an acylation using heptafluoro butyric anhydride (HFBA). The T aliquot was directly derivatized with dansyl chloride to produce the dansyl derivative of 1,2,4-triazole and partitioned into ethyl acetate. All metabolite extracts were then evaporated to dryness, redissolved in acetonitrile/water (30:70, v/v), and analyzed using HPLC with mass spectrometric (MS/MS) detection.

The LOQ was 0.01 ppm for difenoconazole in all stone fruit matrices; the corresponding LOD was 0.000125 ppm. The LOQ (as respective parent equivalents) was 0.01 ppm for the triazole metabolites T, TA, and TAA. The LOD was 0.00003 ppm for T and TA and 0.00005 ppm for TAA in all stone fruit matrices.

The methods were validated in conjunction with the analysis of field trial samples. For concurrent recoveries of difenoconazole, control samples of cherry were fortified at 0.01, 0.10, 1.0, and 1.5 ppm, control samples of peach were fortified at 0.01, 0.10, and 1.0 ppm, and control samples of plum were fortified at 0.01, 0.10, and 2.0 ppm. For concurrent recoveries of the triazole metabolites T and TAA, control samples of cherry and plum were fortified at 0.01 and 0.1 ppm and control samples of peach were fortified at 0.01, 0.1, and 0.5 ppm. For concurrent recoveries of the triazole metabolite TA, control samples of cherry were fortified at 0.025, 0.5, and 1.5 ppm, control samples of peach were fortified at 0.01, 0.1, 0.5, and 1.0 ppm, and control samples of plum were fortified at 0.03 and 0.5 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are reported in Table C.2. Difenoconazole samples were stored at <-10 °C prior to extraction for analysis for 127-442 days (4.2-14.5 months) for tart cherries, 132-441 days (4.3-14.5 months) for sweet cherries, 27-157 days (0.9-5.2 months) for peaches, and 71-427 days (2.3-14.0 months) for plums and triazole metabolite samples were stored for 149-456 days (4.9-15.0 months) for tart cherries, 154-209 days (5.1-6.9 months) for sweet cherries, 14-401 days (0.5-13.2 months) for peaches, and 96-148 days (3.2-4.9 months) for plums. All samples were analyzed within 42 days of extraction; all samples analyzed for residues of difenoconazole *per se* were analyzed within 8 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of peach samples from the subject submission. Available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on tomato are deemed adequate to support the storage intervals and conditions of cherry and plum samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted stone fruit field trial data.

Concurrent method recovery data are presented in Table C.1. The modified LC/MS-MS methods (Syngenta REM 147.08 and Morse Laboratories, Inc. Analytical Method No. 160 Revision 2) used for determining residues of difenoconazole and the triazole metabolites T, TA, and TAA in/on stone fruit (tart cherries, sweet cherries, peaches, and plums) were adequately validated in conjunction with the analysis of field trial samples. Concurrent recoveries were within the acceptable range of 70-120%.

Apparent residues of difenoconazole were <LOQ in/on cherry (tart and sweet), peach, and plum

control samples. The mean residue levels for all metabolites found in the treated samples at the target application rate were similar to the levels found in the untreated samples. Residues of TA in/on control samples of stone fruit were 0.497 to 0.785 ppm for tart cherry, <LOQ to 0.0635 ppm for sweet cherry, <LOQ to 0.530 ppm for peaches, and <LOQ to 0.260 ppm for plums. Residues of TAA in/on control samples of stone fruit were 0.0213 to 0.0570 ppm for tart cherries, <LOQ to 0.0346 ppm for peaches, and <LOQ to 0.0109 ppm for plums. Apparent residues of TAA in/on control samples of sweet cherries were all <LOQ. Apparent residues of T in/on control samples of tart cherries, sweet cherries, peaches, and plums were all <LOQ. The petitioner attributed the occurrence of residues of TA in/on untreated samples to the widespread use of triazoles and the non-specific nature of the common moiety method of analysis. Adequate example chromatograms were provided.

Residue data from the stone fruit trials are reported in Table C.3. A summary of residue data for stone fruit is presented in Table C.4.

Following four broadcast treatment applications of difenoconazole at a total rate of 0.4557-0.4713 lb ai/A, difenoconazole residues were 0.284-0.716 ppm in/on sweet cherry (0 DALA), 0.728-1.01 ppm in/on tart cherry (0 DALA), 0.073-1.02 ppm in/on peach (0 DALA), and 0.070-0.600 ppm in/on plum (0 DALA). Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of sweet cherry, tart cherry, peach, and plum; TA: 0.021-0.106 ppm in/on sweet cherry, 0.236-1.42 ppm in/on tart cherry, <0.01-0.825 ppm in/on peach, and 0.019-0.337 ppm in/on plum; and TAA: <0.01 ppm in/on sweet cherry, 0.011-0.096 ppm in/on tart cherry, <0.01-0.055 ppm in/on peach, and <0.01-0.011 ppm in/on plum.

In the Fresno, CA residue decline trial, residues of difenoconazole *per se* declined slightly at slightly longer post-treatment intervals in/on sweet cherry (Figure C.1.1). For sweet cherry, difenoconazole residues declined from 0.579 ppm (mean) at 0 DALA to 0.546 ppm by 3 DALA and TA residues increased from 0.0623 ppm (mean) at 0 DALA to 0.0630 ppm at 3 DALA. Residues of T and TAA were not detected above the LOQ (0.01 ppm) at any sampling interval.

In the Hughson, CA residue decline trial, residues of difenoconazole *per se* declined slightly at slightly longer post-treatment intervals in/on peach (Figure C.1.2). For peach, difenoconazole residues declined from 0.540 ppm (mean) at 0 DALA to 0.474 ppm by 3 DALA and TA residues declined from 0.0254 ppm at 0 DALA to 0.0229 ppm at 3 DALA.

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Stone Fruit.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)[1]
Cherry	Difenoconazole	0.01	3	93, 97, 87	92 ± 5.0
		0.10	3	104, 94, 72	90 ± 16
		1.0	1	94	NA
		1.5	1	101	NA
	1,2,4-Triazole	0.01	3	98, 86, 104	96 ± 9.2
		0.10	3	93, 98, 91	94 ± 3.6

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Stone Fruit.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)[1]
	Triazole Acetic Acid	0.01	3	97, 96, 88	94 ± 4.9
		0.10	3	101, 97, 95	98 ± 3.1
	Triazole Alanine	0.025	3	88, 93, 78	86 ± 7.6
		0.5	4	102, 87, 91, 89	92 ± 6.7
		1.5	1	98	NA
Peach	Difenoconazole	0.01	4	100, 84, 116, 113	103 ± 15
		0.10	3	104, 87, 91	94 ± 8.9
		1.0	1	112	NA
	1,2,4-Triazole	0.01	4	87, 85, 97, 98	92 ± 6.7
		0.10	3	104, 91, 98	98 ± 6.5
		0.5	1	87	NA
	Triazole Acetic Acid	0.01	4	84, 96, 101, 116	99 ± 13
		0.10	3	94, 97, 95	95 ± 1.5
		0.5	1	101	NA
	Triazole Alanine	0.01	4	90, 89, 104, 98	95 ± 7.1
		0.10	3	93, 92, 97	94 ± 2.6
		0.5	1	89	NA
		1.0	1	91	NA
Plum	Difenoconazole	0.01	5	85, 95, 96, 78, 106	92 ± 11
		0.10	5	80, 99, 100, 93, 107	96 ± 10
		2.0	1	108	NA
	1,2,4-Triazole	0.01	6	91, 90, 71, 80, 84, 70	81 ± 9.1
		0.10	6	94, 92, 96, 92, 88, 94	93 ± 2.7
	Triazole Acetic Acid	0.01	5	96, 96, 89, 104, 93	96 ± 5.5
		0.10	5	92, 94, 96, 95, 95	94 ± 1.5
	Triazole Alanine	0.03	5	91, 93, 81, 90, 84	88 ± 5.1
		0.5	5	89, 87, 89, 90, 88	89 ± 1.1

[1] Standard deviations were calculated only for fortification levels having ≥3 samples.

TABLE C.2. Summary of Storage Conditions.

Matrix	Analyte	Storage Temperature (°C)	Actual Storage Duration[1]	Limit of Demonstrated Storage Stability
Tart Cherry	Difenoconazole	<-10	127-442 days (4.2-14.5 months)	None provided with the subject submission; however, based on previously submitted storage stability data (DP#s 340379 and 356135), when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable at -20°C for up to two years in/on cotton seed, cotton oil, and cotton meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw.
	Triazole metabolites (T, TA, TAA)		149-456 days (4.9-15.0 months)	
Sweet Cherry	Difenoconazole		132-441 days (4.3-14.5 months)	
	Triazole metabolites (T, TA, TAA)		154-209 days (5.1-6.9 months)	
Peach	Difenoconazole		27-157 days (0.9-5.2 months)	
	Triazole metabolites (T, TA, TAA)		14-401 days (0.5-13.2 months)	
Plum	Difenoconazole		71-427 days (2.3-14.0 months)	
	Triazole metabolites (T, TA, TAA)		96-148 days (3.2-4.9 months)	None provided with the subject study; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016).

[1] Interval from harvest to extraction for analysis. Extracts were stored 0-8 days prior to analysis except the plum extracts analyzed for triazole metabolites (T, TA, TAA) from the Lindsay, CA/2008 field trials (W32CA081170) which were stored 42 days prior to analysis.

TABLE C.3. Residue Data from Stone Fruit Field Trials with Difenoconazole.

Trial ID (City, State/Province; Year)	Zone	Crop/ Variety	EP[1]	Total Rate lb ai/A (kg ai/ha)	DALA[2]	Residues (ppm)[3]			
						Difenoconazole	T	TA	TAA
Cherry									
Orefield, PA; 2008 (E04PA081151)	1	Tart Cherry/ Montmorency	Difenoconazole 250EC	0.4557 (0.5108)	0	1.01 0.888	ND ND	1.42 1.20	0.0890 0.0955
Hart, MI; 2008 (C01MI081172)	5	Tart Cherry/ Mt. Montmorency	Difenoconazole 250EC	0.4675 (0.5241)	0	0.804 0.728	ND ND	0.468 0.236	0.0234 0.0113
Fresno, CA; 2008 (W29CA081153)[4]	10	Sweet Cherry/ Brooks	Difenoconazole 250EC	0.4713 (0.5283)	0	0.664 0.494	ND ND	0.0660 0.0585	<0.01 <0.01
					1	0.582	ND	0.0600	<0.01
					3	0.546	ND	0.0630	<0.01
Kerman, CA; 2008 (W30CA081154)	10	Sweet Cherry/ Brooks	Difenoconazole 250EC	0.4619 (0.5178)	0	0.300 0.284	ND ND	0.0620 0.0670	<0.01 <0.01
Ephrata, WA; 2008 (W18WA081155)	11	Sweet Cherry/ Bing	Difenoconazole 250EC	0.4650 (0.5213)	0	0.716 0.672	ND ND	0.0232 0.0211	<0.01 <0.01
Ephrata, WA; 2008 (W18WA081156)	11	Sweet Cherry/ Bing	Difenoconazole 250EC	0.4612 (0.5170)	0	0.456 0.448	ND ND	0.0975 0.106	<0.01 <0.01
Peach									
Alton, NY; 2009 (E031175NY08)	1	Peach/ Catherina	Difenoconazole 250EC	0.4613 (0.5171)	0	0.251 0.319	ND ND	0.138 0.146	<0.01 <0.01
Alto, GA; 2009 (E121176GA08)	2	Peach/ Georgia Belle	Difenoconazole 250EC	0.4605 (0.5162)	0	0.354 0.314	ND ND	0.695 0.825	0.0545 0.0535
Pikeville, NC; 2009 (E101177NC08)	2	Peach/ New Haven	Difenoconazole 250EC	0.4612 (0.5170)	0	0.880 1.02	<0.01 ND	0.0555 0.0498	<0.01 <0.01
Athens, GA; 2008 (E12GA081160)	2	Peach/ Contender	Difenoconazole 250EC	0.4641 (0.5203)	0	0.672 0.872	ND ND	0.0715 0.0975	<0.01 <0.01
Branchton, Ontario, Canada; 2008 (C32CAN081173)	5	Peach/ Red Haven	Difenoconazole 250EC	0.4616 (0.5175)	0	0.135 0.130	ND ND	<0.01 <0.01	ND ND
D'Hanis, TX; 2008 (W07TX081162)	6	Peach/ La Feliciana	Difenoconazole 250EC	0.4568 (0.5121)	0	0.652 0.414	ND ND	0.150 0.153	0.0281 0.0232
Hughson, CA; 2008 (W26CA081163)[4]	10	Peach/ Fairtimes	Difenoconazole 250EC	0.4632 (0.5192)	0	0.538 0.542	ND ND	0.0254 0.0254	<0.01 <0.01
					1	0.238	ND	0.0265	<0.01
					3	0.474	ND	0.0229	<0.01
Madera, CA; 2008 (W30CA081164)	10	Peach/ Angelas	Difenoconazole 250EC	0.4597 (0.5153)	0	0.0728 0.0820	ND ND	0.0187 0.0216	<0.01 <0.01
Kingsburg, CA; 2008 (W32CA081165)	10	Peach/ Ryan Sun	Difenoconazole 250EC	0.4869 (0.5458)	0	0.129 0.195	ND ND	0.0142 0.0190	<0.01 <0.01
Plum									
Hart, MI; 2008 (C01MI081174)	5	Plum/ Stanley	Difenoconazole 250EC	0.4568 (0.5121)	0	0.358 0.253	ND ND	0.257 0.337	0.0110 0.0114
Hughson, CA; 2008 (W26CA081167)	10	Plum/ French Plum	Difenoconazole 250EC	0.4638 (0.5199)	0	0.486 0.600	ND ND	0.0443 0.0448	<0.01 <0.01
Fresno, CA; 2008 (E19CA081168)	10	Plum/ Owen-T	Difenoconazole 250EC	0.4582 (0.5136)	0	0.127 0.0700	ND ND	0.0452 0.0440	<0.01 <0.01

TABLE C.3. Residue Data from Stone Fruit Field Trials with Difenoconazole.

Trial ID (City, State/Province; Year)	Zone	Crop/ Variety	EP[1]	Total Rate lb ai/A (kg ai/ha)	DALA[2]	Residues (ppm)[3]			
						Difenoconazole	T	TA	TAA
Kerman, CA; 2008 (W29CA081169)	10	Plum/ French Prune	Difenoconazole 250EC	0.4614 (0.5172)	0	0.0816 0.130	ND ND	0.0187 0.0205	<0.01 <0.01
Lindsay, CA; 2008 (W32CA081170)	10	Plum/ Angelina's	Difenoconazole 250EC	0.4591 (0.5147)	0	0.316 0.326	ND ND	0.100 0.120	<0.01 <0.01
Forest Grove, OR; 2008 (C23MO081263)	12	Plum/ Late Italian	Difenoconazole 250EC	0.4603 (0.5160)	0	0.372 0.426	ND ND	0.191 0.185	<0.01 <0.01

[1] End use product; 2.08 lb/gal EC formulation.
[2] DALA = Days after last application.
[3] The validated LOQ was 0.01 ppm. TA = triazole alanine. TAA = triazole acetic acid. T = 1,2,4-triazole. ND = Not detected.
[4] Samples were taken at additional sampling intervals for a residue decline study.

TABLE C.4. Summary of Residue Data from Crop Field Trials with Difenoconazole.

Commodity	Total Applic. Rate lb ai/A (kg ai/ha)	DALA[1]	Residue Levels (ppm)[2]						
			n	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Difenoconazole									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	0.284	0.716	0.694	0.475	0.504	0.167
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	0.728	1.01	0.949	0.846	0.858	0.121
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	0.0728	1.02	0.950	0.337	0.421	0.298
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	0.070	0.600	0.543	0.321	0.295	0.168
T									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	<0.01	<0.01	<0.01	<0.01	<0.01	NA
TA									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	0.0211	0.106	0.102	0.064	0.063	0.030
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	0.236	1.42	1.31	0.834	0.831	0.568
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	<0.01	0.825	0.760	0.053	0.140	0.232
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	0.0187	0.337	0.297	0.0726	0.117	0.104
TAA									
Sweet Cherry	0.4612-0.4713 (0.5170-0.5283)	0	8	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Tart Cherry	0.4557-0.4675 (0.5108-0.5241)	0	4	0.0113	0.0955	0.0923	0.0562	0.055	0.044

TABLE C.4. Summary of Residue Data from Crop Field Trials with Difenoconazole.

Commodity	Total Applic. Rate lb ai/A (kg ai/ha)	DALA [1]	Residue Levels (ppm)[2]						
			n	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Peach	0.4568-0.4869 (0.5121-0.5458)	0	18	<0.01	0.0545	0.054	0.010	0.017	0.015
Plum	0.4568-0.4638 (0.5121-0.5199)	0	12	<0.01	0.0114	0.0112	0.010	0.010	0.000

[1] DALA = Days after last application.
[2] TA = triazole alanine. TAA = triazole acetic acid. T = 1,2,4-triazole. Mean, median, HAFT, and standard deviations were calculated by the reviewer. The LOQ (0.01 ppm for all analytes) was used for calculations for any results reported as <LOQ in Table C.3. Does not include additional sampling intervals collected for the residue decline study.
[3] HAFT = Highest Average Field Trial

Figure C.1.1 Residue Decline of Difenoconazole in Cherry (Fresno, CA trial).

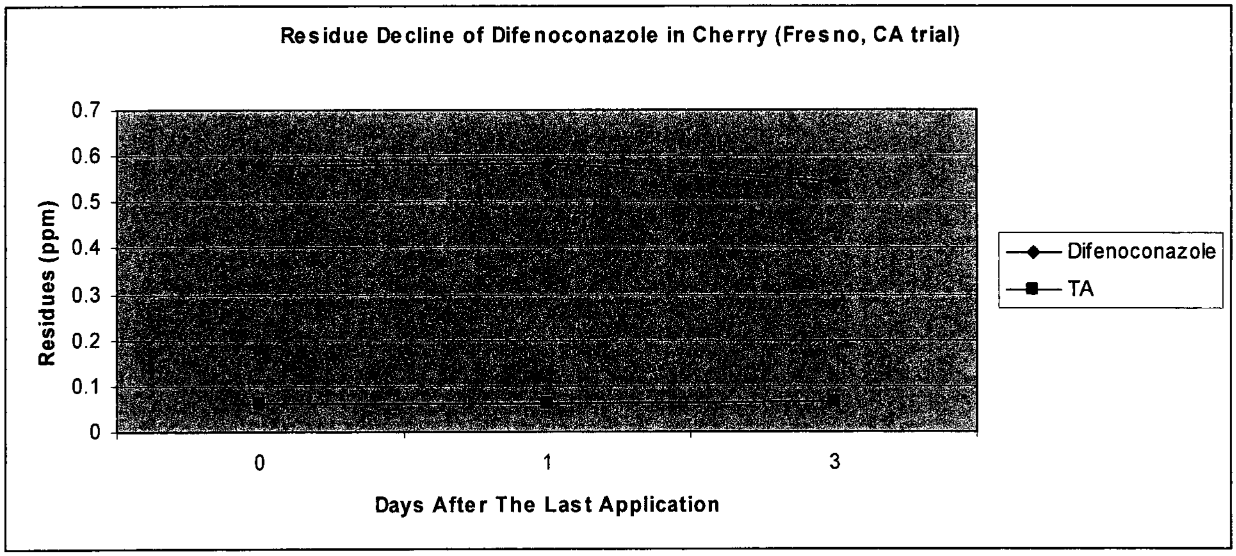


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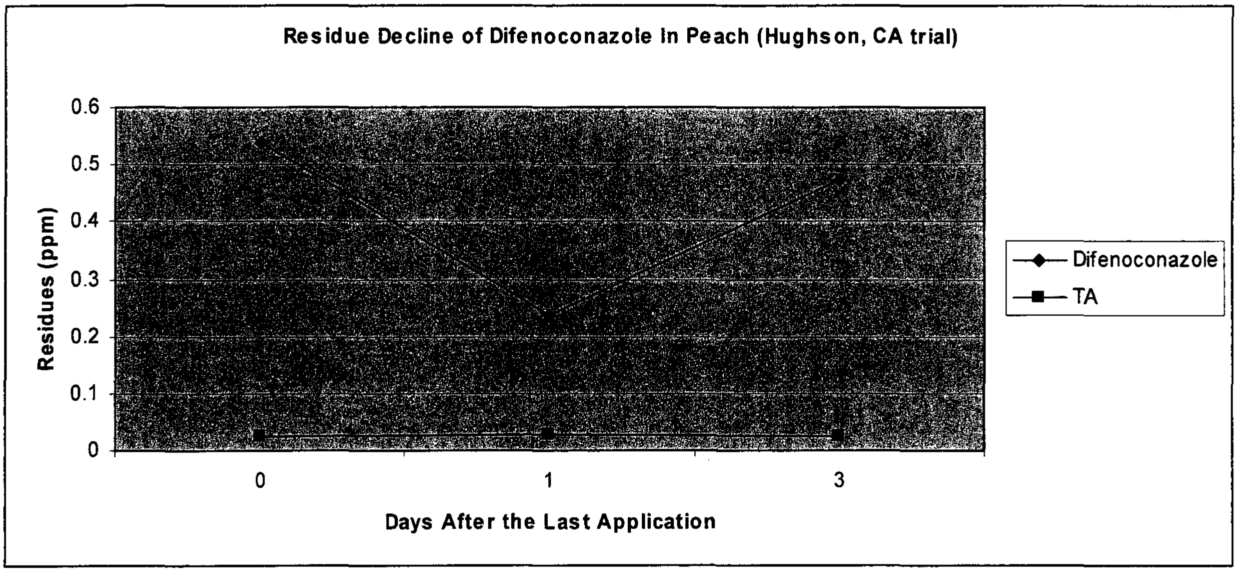
Figure C.1.2 Residue Decline of Difenoconazole in Peach (Hughson, CA trial).



D. CONCLUSION

The field trial data reflect the use of difenoconazole (EC formulation) as four foliar broadcast applications at a nominal rate of 0.115 lb ai/A (0.129 kg ai/ha) per application for a total seasonal rate of 0.46 lb ai/A (0.516 kg ai/ha). The data reflect RTIs of 5-8 days and 0 days PHI for stone fruit (tart cherry, sweet cherry, peach, and plum). Additional samples were collected at 0, 1, and 3 DALA from two trials to assess residue decline.

Acceptable methods were used for the determination of residues of difenoconazole and the triazole metabolites. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of peach samples from the subject submission. Available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on tomato are deemed adequate to support the storage intervals and conditions of cherry and plum samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted stone fruit field trial data.

There was no unusual weather conditions reported that may have adversely impacted the results of the study. Additionally, it does not appear that the agricultural practices used adversely impacted the results of the study.

E. REFERENCES

DP#:	172067 and 178394
Subject:	PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS# 9029, 9895.
From:	R. Lascola
To:	J. Stone/C. Giles-Parker
Dated:	10/26/92
MRIDs:	42090001-42090004, 42090032-42090059, and 42303901

DP#:	340379
Subject:	PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From:	W. Wassell/M. Sahafeyan
To:	D. Rosenblatt/S. Brothers
Dated:	8/9/07
MRIDs:	46950215-46950237

DP#	356135
Subject:	Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	J. Bazuin/T. Kish
Dated:	9/17/09
MRIDs:	47413501 and 47413502

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number(s): 9F7676
DP # 378829
PC Code: 128847

Template Version June 2005.

Primary Evaluator: Bonnie Cropp-Kohlligian, Environmental Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Bonnie Cropp-Kohlligian

Approved by: Susan V. Hummel, Chemist/Senior Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Susan V. Hummel

This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted (1/06/2011). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47929803. Willard, T.; Mayer, T. (2009) Difenoconazole - Magnitude of the Residues in or on Sweet or Tart Cherry, Peach, and Plum as Representative Commodities of Fruit, Stone, Group 12: Final Report. Project Number: T002402-07, ML08-1479-SYN. Unpublished study prepared by Syngenta Crop Protection, Inc. 413 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection, Inc. submitted processing studies for difenoconazole on plums. In two crop field trials conducted in CA, an emulsifiable concentrate (EC) formulation of difenoconazole was applied four times to plums at the label rate (1x) of 0.115 lb ai/A/application for a total nominal application rate of 0.46 lb ai/A (actual application rates of 0.4614-0.4638 lb ai/A) and at an exaggerated rate (3.5x) of 0.403 lb ai/A/application, for a total nominal application rate of 1.6 lb ai/A (actual application rates of 1.622-1.637 lb ai/A). The re-treatment intervals were 7-8 days. Plum fruit were harvested at 0 day pre-harvest intervals (PHI) and processed into prunes by ACDS Research (North Rose, NY) using simulated commercial procedures. Adequate descriptions were provided of the processing procedures, including material balance summaries.

Samples were analyzed for residues of difenoconazole using modified method Syngenta REM 147.08, "Residue Method for the Determination of Residues of Difenoconazole (CGA-169374) in Various Crops and Processed Crop Fractions" using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Additionally, residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) were measured using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". The limit of quantitation (LOQ) was 0.01 ppm for each analyte in all matrices. The methods were adequate for data collection based on concurrent method recoveries.

The maximum storage duration of difenoconazole samples from harvest/processing to extraction for analysis was 105 days (3.5 months) for plum fruit (RAC) and 426 days (14.0 months) for prune. The maximum storage duration of triazole metabolite samples from harvest/processing to extraction for analysis was 147 days (4.8 months) for plum fruit (RAC) and 427 days (14.0 months) for prune. Analysis took place between 0 and 6 days after extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year and in all processed commodities for at least two years, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of plum fruit and prune samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted plum processing data.

Concentration following processing at the label rate (1x) and exaggerated rate (3.5x the field application rate) was observed in prunes. In the 1x trials, residues of difenoconazole were 0.0924-0.644 ppm for plum fruit (RAC) and 0.302-1.07 ppm for prunes (resulting in processing factors of 1.9-2.9x). Residues of metabolite TA were 0.0162-0.0432 ppm for plum fruit (RAC) and 0.0488-0.115 ppm for prunes (resulting in processing factors of 2.3-3.0x). Residues of metabolites T and TAA were each below the LOQ (<0.01 ppm for all analytes) in/on all samples of plum fruit and prunes. Therefore, no processing factors were calculated. In the 3.5x trials, residues of difenoconazole were 0.424-1.74 ppm for plum fruit (RAC) and 1.11-4.64 ppm for prunes (resulting in processing factors of 2.7x). Residues of metabolite TA were 0.0424-0.0620 ppm for plum fruit (RAC) and 0.0975-0.144 ppm for prunes (resulting in processing factors of 2.2-2.3x). With the exception of one replicate of TAA in prune (0.0102 ppm) residues of metabolites T and TAA were each below the LOQ (<0.01 ppm for all analytes) in/on all samples of plum fruit and prunes. Therefore, no processing factors were calculated. All of the processing factors calculated in this study were less than the maximum theoretical concentration factor of 3.4x for prunes (based on loss of water; OPPTS 860.1520, Table 2).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# 378829].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: soil characterization, weather data, maintenance chemical applications, irrigation practices, field history records, tank mix storage stability data, and field samples weights were not collected under GLP. These deviations did not impact the validity of the study.

A. BACKGROUND INFORMATION

Difenoconazole is a broad-spectrum fungicide which belongs to the triazole (including the conazole) class of chemicals. It was developed under the code number CGA-169374.

The chemical structure and nomenclature of difenoconazole and the triazole metabolites are presented in Table A.1. The physicochemical properties of the technical grade of difenoconazole are presented in Table A.2.

TABLE A.1. Test Compound Nomenclature.

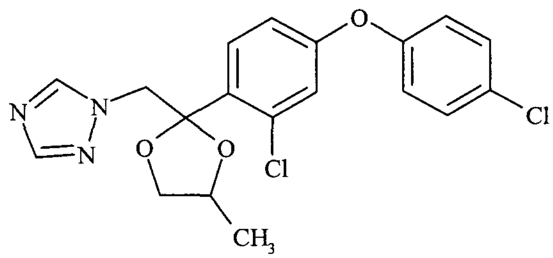
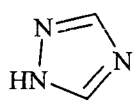
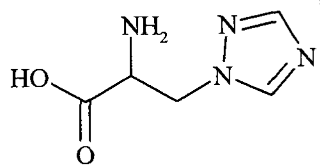
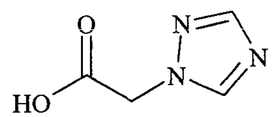
Compound			
Common name	Difenoconazole		
Company experimental name	CGA-169374		
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole		
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole		
CAS registry number	119446-68-3		
End-use product (EP)	Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole (Inspire®; EPA Reg. No. 100-1262)		
Compound			
Chemical name	Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

TABLE A.2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	

TABLE A.2. Physicochemical Properties of Difenoconazole.		
Parameter	Value	Reference
Solvent solubility	g/100 mL at 25 °C: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5×10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, $Log(K_{OW})$	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

B. EXPERIMENTAL DESIGN

Two field trials were conducted in CA. Test plots were treated with Difenoconazole 250EC, containing 2.08 lb/gal difenoconazole in an emulsifiable concentrate (EC) formulation. Plums were treated with four foliar broadcast applications at 1x the target label rate of 0.115 lb ai/A (total seasonal rate of 0.46 lb ai/A) and at 3.5x the target label rate of 0.403 lb ai/A (total seasonal rate of 1.6 lb ai/A). Applications were made at re-treatment intervals of 7-8 days. The actual trial use patterns are reported in Table B.1.2.

B.1. Application and Crop Information

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information				Total Rate lb ai/A	Tank Mix/ Adjuvants[4]
		Method; Timing (Crop growth stage)	Volume[2] GPA (l/ha)	Rate lb ai/A (kg ai/ha)	RTI[3] (days)		
Hughson, CA; 2008 (W26CA081167p)	Difenoconazole 250EC	1. Foliar broadcast; BBCH 81, beginning to ripen	171.21 (1,601.50)	0.1169 (0.1310)	-	0.4638 (0.5199)	COC at 0.375% v/v
		2. Foliar broadcast; BBCH 88, fruit beginning to soften	158.17 (1,479.52)	0.1147 (0.1286)	8		
		3. Foliar broadcast; BBCH 88, fruit beginning to soften	160.26 (1,499.07)	0.1162 (0.1303)	7		
		4. Foliar broadcast; BBCH 89, fully ripe	159.96 (1,496.27)	0.1160 (0.1300)	7		
Hughson, CA; 2008 (W26CA081167p)	Difenoconazole 250EC	1. Foliar broadcast; BBCH 81, beginning to ripen	163.86 (1,532.75)	0.4051 (0.4541)	-	1.6222 (1.8185)	COC at 0.375% v/v
		2. Foliar broadcast; BBCH 88, fruit beginning to soften	156.36 (1,462.59)	0.4066 (0.4558)	8		
		3. Foliar broadcast; BBCH 88, fruit beginning to soften	160.70 (1,503.19)	0.4042 (0.4531)	7		
		4. Foliar broadcast; BBCH 89, fully ripe	156.26 (1,461.66)	0.4063 (0.4555)	7		
Kerman, CA; 2008 (W26CA081169p)	Difenoconazole 250EC	1. Foliar broadcast; BBCH 79	174.30 (1,630.40)	0.116 (0.1300)	-	0.4614 (0.5172)	NIS at 0.15% v/v
		2. Foliar broadcast; BBCH 87	172.57 (1,614.22)	0.1150 (0.1289)	7		
		3. Foliar broadcast; BBCH 88	172.42 (1,612.82)	0.1150 (0.1289)	7		
		4. Foliar broadcast; BBCH 89	173.38 (1,621.80)	0.1154 (0.1294)	7		
Kerman, CA; 2008 (W26CA081169p)	Difenoconazole 250EC	1. Foliar broadcast; BBCH 79	173.36 (1,621.61)	0.4104 (0.4601)	-	1.6373 (1.8354)	NIS at 0.15% v/v
		2. Foliar broadcast; BBCH 87	173.32 (1,621.24)	0.4101 (0.4597)	7		
		3. Foliar broadcast; BBCH 88	171.72 (1,606.27)	0.4060 (0.4551)	7		
		4. Foliar broadcast; BBCH 89	173.72 (1,624.98)	0.4108 (0.4605)	7		

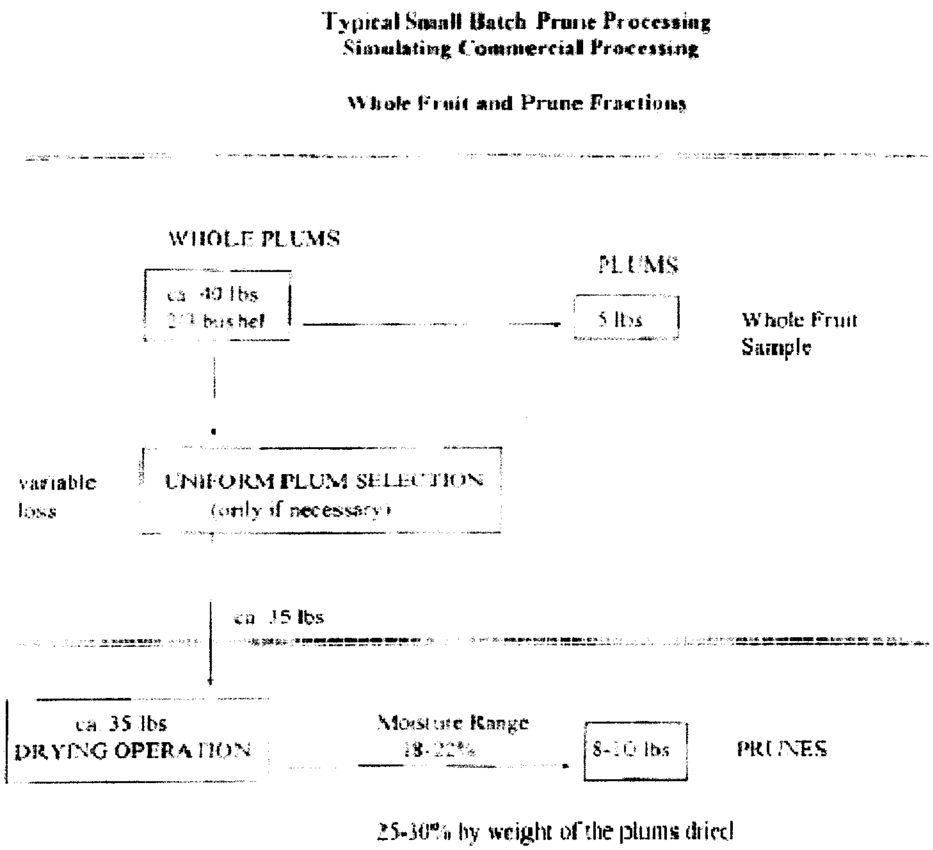
1 EP = End-use Product; an emulsifiable concentrate (EC) difenoconazole formulation containing 2.08 lb ai/gal.
2 GPA = gallons per acre; liters per hectare.
3 RTI = Retreatment Interval.
4 NIS = Non-ionic surfactant. COC = Crop oil concentrate.

B.2. Sample Handling and Processing Procedures

Composite samples of plum fruit from the control and treated plots were collected on the day of the last application (0 DALA) and shipped ambient to ACDS (North Rose, NY) for processing into prunes. After processing, samples were shipped on dry ice to Syngenta Crop Protection, Inc. (Greensboro, NC) for preparation. Samples of plum fruit (RAC) and prunes were ground with dry ice in a Hobart foodcutter. After preparation, samples were shipped frozen to Morse Laboratories, LLC (Sacramento, CA) for analysis. At the analytical laboratory samples were stored in temperature-monitored freezers at -20 ± 5 °C until analysis.

The processing procedure simulated commercial operations of plum production as closely as possible to generate the required fraction of plum fruit (RAC) and prunes, with some variations to commercial methods. A processing flowchart for plums, copied without alteration from MRID 47929803, is presented below in Figure 1.

FIGURE 1. Processing Flowchart for Plums.



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B.3. Analytical Methodology

Samples of plum fruit (RAC) and its processed fraction (prunes) were analyzed for residues of difenoconazole with modified analytical method Syngenta REM 147.08 titled "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS". Additionally, stone fruit samples were analyzed for residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". Both methods have been reviewed previously by HED (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan). Brief descriptions of the methods were included in the submission.

Residues of difenoconazole in plum samples were extracted by refluxing with methanol/concentrated ammonium hydroxide (80:20, v:v). Aliquots of the extracts were diluted with ultra-pure water, cleaned up using solid phase extraction, and analyzed using high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). Residues of metabolites T, TA, and TAA were extracted with methanol/water (80:20, v/v). Following the addition of Celite, the extracts were vacuum filtered, rinsed, and brought to volume with methanol/water (80:20, v:v). Aliquots of the TAA extract were purified by solid phase extraction and then derivatized by HCl/butanol esterification. The TA aliquot underwent two derivatizations: an esterification using HCL/butanol and an acylation using heptafluoro butyric anhydride (HFBA). The T aliquot was directly derivatized with dansyl chloride to produce the dansyl derivative of 1,2,4-triazole and partitioned into ethyl acetate. All metabolite extracts were then evaporated to dryness, redissolved in acetonitrile/water (30:70, v/v), and analyzed using HPLC with mass spectrometric (MS/MS) detection.

The LOQ was 0.01 ppm for difenoconazole in all plum matrices; the corresponding LOD was 0.000125 ppm. The LOQ (as respective parent equivalents) was 0.01 ppm for the triazole metabolites T, TA, and TAA. The LOD was 0.00003 ppm for T and TA and 0.00005 ppm for TAA in all plum matrices.

The methods were validated in conjunction with the analysis of processing samples. For concurrent recoveries of difenoconazole, control samples of plum fruit (RAC) were fortified at 0.01, 0.10, and 2.0 ppm and control samples of prunes were fortified at 0.01, 0.10, 2.0, and 5.0 ppm. For concurrent recoveries of the triazole metabolites T and TAA, control samples of plum fruit and prunes were fortified at 0.01 and 0.10 ppm. For concurrent recoveries of the triazole metabolite TA, control samples of plum fruit were fortified at 0.03 and 0.5 ppm and control samples of prunes were fortified at 0.05 and 0.5 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are summarized in Table C.2. After processing, samples were stored frozen (-10 °C) until analysis. The maximum storage duration of difenoconazole samples from harvest/processing to extraction for analysis was 105 days (3.5 months) for plum fruit (RAC) and 426 days (14.0 months) for prune. The maximum storage duration of triazole metabolite samples from harvest/processing to extraction for analysis was 147 days (4.8 months) for plum fruit (RAC) and 427 days (14.0 months) for prune. Analysis took place between 0 and 6 days after extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year and in all processed commodities for at least two years, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of plum fruit and prune samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted plum processing data.

Concurrent method recovery data are presented in Table C.1. The modified LC/MS-MS methods (Syngenta REM 147.08 and Morse Laboratories, Inc. Analytical Method No. 160 Revision 2) used for determining residues of difenoconazole and the triazole metabolites T, TA, and TAA in/on plum fruit RAC and its processed fraction were adequately validated in conjunction with the analysis of field trial samples. Concurrent recoveries were within the acceptable range of 70-120%.

Apparent residues of difenoconazole, T, and TAA were <LOQ in/on control samples of plum fruit (RAC) and prunes. Apparent residues of TA in/on control samples of plum were <LOQ to 0.0199 ppm for fruit (RAC) and 0.0268 to 0.0333 ppm for plum. The petitioner attributed the occurrence of residues of TA in/on untreated samples to the widespread use of triazoles and the non-specific nature of the common moiety method of analysis. Adequate example chromatograms were provided.

Residue data from the 1x and 3.5x plum processing studies are reported in Table C.3.

In the 1x trials, residues of difenoconazole were 0.0924-0.644 ppm for plum fruit (RAC) and 0.302-1.07 ppm for prunes (resulting in processing factors of 1.9-2.9x). Residues of metabolite TA were 0.0162-0.0432 ppm for plum fruit (RAC) and 0.0488-0.115 ppm for prunes (resulting in processing factors of 2.3-3.0x). Residues of metabolites T and TAA were each below the LOQ (<0.01 ppm for all analytes) in/on all samples of plum fruit and prunes. Therefore, no processing factors were calculated.

In the 3.5x trials, residues of difenoconazole were 0.424-1.74 ppm for plum fruit (RAC) and 1.11-4.64 ppm for prunes (resulting in processing factors of 2.7x). Residues of metabolite TA were 0.0424-0.0620 ppm for plum fruit (RAC) and 0.0975-0.144 ppm for prunes (resulting in processing factors of 2.2-2.3x). With the exception of one replicate of TAA in prune (0.0102 ppm) residues of metabolites T and TAA were each below the LOQ (<0.01 ppm for all analytes) in/on all samples of plum fruit and prunes. Therefore, no processing factors were calculated. All of the processing factors calculated in this study were less than the maximum theoretical concentration factor of 3.4x for prunes (based on loss of water; OPPTS 860.1520, Table 2).

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Plum and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)[1]
Fruit (RAC)	Difenoconazole	0.01	5	85, 95, 96, 78, 106	92 ± 11
		0.10	5	80, 99, 100, 93, 107	96 ± 10
		2.0	1	108	NA
	1,2,4-Triazole	0.01	6	91, 90, 71, 80, 84, 70	81 ± 9.1
		0.10	6	94, 92, 96, 92, 88, 94	93 ± 2.7
	Triazole Acetic Acid	0.01	5	96, 96, 89, 104, 93	96 ± 5.5
		0.10	5	92, 94, 96, 95, 95	94 ± 1.5
	Triazole Alanine	0.03	5	91, 93, 81, 90, 84	88 ± 5.1
		0.5	5	89, 87, 89, 90, 88	89 ± 1.1
Prune	Difenoconazole	0.01	2	81, 106	94
		0.10	1	91	NA
		2.0	1	97	NA
		5.0	1	104	NA
	1,2,4-Triazole	0.01	2	93, 77	85
		0.10	2	91, 96	94
	Triazole Acetic Acid	0.01	2	90, 102	96
		0.10	2	91, 90	91
	Triazole Alanine	0.05	2	78, 93	86
		0.5	2	82, 90	86

[1] Standard deviations were calculated only for fortification levels having ≥3 samples.

TABLE C.2. Summary of Storage Conditions.

Matrix	Analyte	Storage Temperature (°C)	Actual Storage Duration[1]	Limit of Demonstrated Storage Stability
Fruit (RAC)	Difenoconazole	<-10	100-105 days	None provided with the subject submission; however, based on previously submitted storage stability data (DP#s 340379 and 356135), when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable at -20°C for up to two years in/on cotton seed, cotton oil, and cotton meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw. Although the available storage stability data are not sufficiently representative for all processed commodities, which usually requires an oilseed, a fruit/fruiting vegetable, and a non-oily grain, when taken as a whole, the available data are deemed adequate to demonstrate the stability of residues of difenoconazole *per se* in all processed commodities for up to two years when stored under frozen conditions.
	Triazole metabolites (T, TA, TAA)		114-147 days	
Prune	Difenoconazole		106-426 days	
	Triazole metabolites (T, TA, TAA)		113-427 days	None provided with the subject study; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016).

[1] Interval from harvest/processing to extraction for analysis. Extracts were stored 0-6 days prior to analysis. Samples were stored 2 to 8 days before processing.

TABLE C.3. Residue Data from Plum Processing Studies with Difenoconazole.

RAC	Processed Commodity	Total Rate lb ai/A (kg ai/ha)	DALA	Residues (ppm)				Processing Factor[1,2]			
				Difenoconazole	T	TA	TAA	Difenoconazole	T	TA	TAA
1x Trial - Hughson, CA; 2008 (W26CA081167p)											
Plum	Fruit (RAC)	0.4638 (0.5199)	0	0.448 0.454 0.644	ND ND ND	0.0432 0.0396 0.0416	<0.01 <0.01 <0.01	--	--	--	--
	Prune			1.07 0.872 1.06	ND ND ND	0.0765 0.0965 0.115	<0.01 <0.01 <0.01	1.9x	NC	2.3x	NC
1x Trial - Kerman, CA; 2008 (W26CA081169p)											
Plum	Fruit (RAC)	0.4614 (0.5172)	0	0.116 0.146 0.0924	ND ND ND	0.0192 0.0162 0.0179	<0.01 <0.01 <0.01	--	--	--	--
	Prune			0.342 0.380 0.302	ND ND ND	0.0490 0.0488 0.0615	<0.01 <0.01 <0.01	2.9x	NC	3.0x	NC
3.5x Trial - Hughson, CA; 2008 (W26CA081167p)											
Plum	Fruit (RAC)	1.622 (1.818)	0	1.06 1.61 1.74	ND ND ND	0.0476 0.0620 0.0620	<0.01 <0.01 <0.01	--	--	--	--
	Prune			4.64 3.66 3.80	ND ND ND	0.117 0.140 0.144	<0.01 0.0102 <0.01	2.7x	NC	2.3x	NC
3.5x Trial - Kerman, CA; 2008 (W26CA081169p)											
Plum	Fruit (RAC)	1.637 (1.835)	0	0.576 0.424 0.436	ND ND ND	0.0515 0.0472 0.0424	<0.01 <0.01 <0.01	--	--	--	--
	Prune			1.11 1.57 1.22	ND ND ND	0.115 0.0975 0.0985	<0.01 <0.01 <0.01	2.7x	NC	2.2x	NC
Average											
Plum	Prune (1x)							2.4x	NC	2.7x	NC
	Prune (3.5x)							2.7x	NC	2.3x	NC

[1]NC = Not calculated; residues were below the LOQ (<0.01 ppm for all in analytes) in both the RAC and processed fraction.
[2] Processing Factor = [Measured residue for analyte in the processed fraction] / [Measured residue for analyte in the RAC].

D. CONCLUSION

The processing data for plums indicate that residues of difenoconazole and its metabolite TA concentrate in prunes (~2-3x). Metabolites T and TAA are not likely to concentrate in plum processed commodities because residues in processed commodities were below the residues found in/on prunes following four applications of the EC formulation at the label rate (1x) of 0.46 lb ai/A (0.516 kg ai/ha) and the exaggerated 3.5x rate of 1.6 lb ai/A (1.80 kg ai/ha).

Acceptable methods were used for the determination of residues of difenoconazole and the triazole metabolites. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year and in all processed commodities for at least two years, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of plum fruit and prune samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted plum processing data.

E. REFERENCES

DP#:	172067 and 178394
Subject:	PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS# 9029, 9895.
From:	R. Lascola
To:	J. Stone/C. Giles-Parker
Dated:	10/26/92
MRIDs:	42090001-42090004, 42090032-42090059, and 42303901

DP#:	340379
Subject:	PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From:	W. Wassell/M. Sahafeyan
To:	D. Rosenblatt/S. Brothers
Dated:	8/9/07

DP#	356135
Subject:	Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	J. Bazuin/T. Kish
Dated:	9/17/09
MRIDs:	47413501 and 47413502

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number(s): 9F7676
DP # 378829
PC Code: 128847

Template Version June 2005

Primary Evaluator: Bonnie Cropp-Kohlligian, Environmental Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Bonnie Cropp-Kohlligian

Approved by: Susan V. Hummel, Chemist/Senior Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Susan V. Hummel

This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted (1/06/2011). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47929804. Willard, T. and T. Mayer, (2009) Difenoconazole - Magnitude of the Residue in or on Carrot. Final Report. Study Number T002431-07. Unpublished study prepared by Syngenta Crop Protection, Inc. 181 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection, Inc. has submitted crop field trial data for difenoconazole in/on carrots. Eight carrot field trials were conducted in the United States encompassing Zones 3 (FL; 1 trial), 5 (ND; 1 trial), 6 (TX; 1 trial), 10 (CA; 4 trials), and 11 (ID; 1 trial) during the 2008 and 2009 growing seasons. Each trial site consisted of one untreated plot and one treated plot. Each treated plot received four foliar broadcast applications of a 2.08 lb/gal emulsifiable concentrate (EC) formulation of difenoconazole at ~0.115 lb ai/A per application, with a 5- to 8-day retreatment interval, for a total seasonal rate of ~0.460 lb ai/A. Applications were made using ground equipment, in ~16-49 gal/A spray volumes, using either a non-ionic surfactant or crop oil concentrate as an adjuvant with one exception. No adjuvant was added to the first treatment at the ID trial. Carrot root samples were harvested 7 days after the last application (DALA). At one trial site (Fresno, CA), samples were also collected at 0, 3, 7, 10, and 14 DALA to assess residue decline.

Samples of carrots were analyzed for residues of difenoconazole using modified method Syngenta REM 147.08, "Residue Method for the Determination of Residues of Difenoconazole (CGA-169374) in Various Crops and Processed Crop Fractions" using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Additionally, residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) were measured using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". The limit of quantitation (LOQ) was 0.01 ppm for each analyte in all matrices. The methods were adequate for data collection based on concurrent method

recoveries.

The maximum storage duration from sampling to analysis was 381 days (12.5 months) for difenoconazole analysis and 356 days (11.7 months) for triazole metabolite analysis. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on potato tubers are deemed adequate to support the storage intervals and conditions of carrot samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted carrot field trial data.

Following four broadcast foliar applications of the EC formulation of difenoconazole plus adjuvant at a total application rate of 0.461-0.472 lb ai/A, residues of difenoconazole ranged from <LOQ (0.01 ppm) to 0.203 ppm in/on carrots at a 7-day PHI. Residues of 1,2,4-T were below the LOQ in/on all samples of carrots harvested 7 days following treatment. Residues of TA and TAA in/on carrot samples harvested at a 7-day PHI ranged 0.012-0.054 ppm and <0.01-0.013 ppm, respectively.

Residue decline data show that residues of difenoconazole were relatively stable from the 0-day to 7-day sampling interval and then declined to <LOQ (0.01 ppm) by the 10-day sampling interval. Residues of 1,2,4-T and TAA were at or near the LOQ (0.01 ppm) in/on all samples from the residue decline trial. Residues of TA in carrots fluctuated over the 14 day sampling period (ranging from 0.024 to 0.054 ppm) with no definite pattern of decline or accumulation.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP# 378829].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. The study described was conducted to meet the requirements of EPA Good Laboratory Practice Standards (40 CFR Part 160) with the following exceptions:

- Weather data were not collected or recorded under GLP;
- Spray mix storage stability data were not generated as required;
- Maintenance chemicals and irrigation were not applied under GLP;
- Soil characterization was not conducted under GLP.

A. BACKGROUND INFORMATION

Difenoconazole is a broad-spectrum fungicide which belongs to the triazole (including the conazole) class of chemicals. It was developed under the code number CGA-169374.

The chemical structure and nomenclature of difenoconazole and the triazole metabolites are presented in Table A.1. The physicochemical properties of the technical grade of difenoconazole are presented in Table A.2.

TABLE A.1. Test Compound Nomenclature.

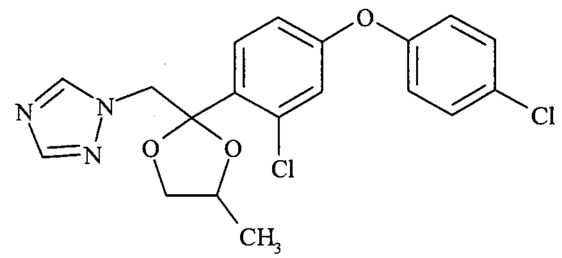
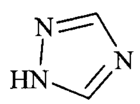
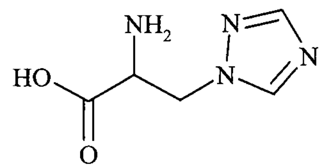
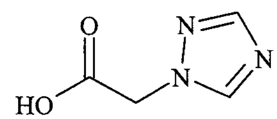
Compound			
Common name	Difenoconazole		
Company experimental name	CGA-169374		
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole		
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole		
CAS registry number	119446-68-3		
End-use product (EP)	Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole (Inspire®; EPA Reg. No. 100-1262)		
Compound			
Chemical name	Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

TABLE A.2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	

TABLE A.2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Solvent solubility	g/100 mL at 25 °C: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5×10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, $Log(K_{OW})$	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

The test site conditions are summarized in Table B.1.1 and the study use patterns are summarized in Table B.1.2. Refer to Table B.1.3 for a summary of the number of field trials and geographical locations.

TABLE B.1.1 Trial Site Conditions.

City, State; Year (Trial Identification)	Soil characteristics			
	Type	%OM	pH	CEC (meq/100 g)
Jennings, FL; 2009 (E13GA081181)	Loamy sand	3.7	6.1	11.6
Gardner, ND 2008 (C12ND081182	Clay loam	3.6	7.8	30.5
Madera, CA 2008 (W30CA081184)	Sandy loam	1.15	7.5	5.7
Madera, CA 2008 (W29CA081185)	Loamy sand	0.5	8.2	6.9
Fresno, CA 2008 (W30CA081186)	Sandy loam	0.8	7.4	6.9
Los Alamos, CA 2008 (W27CA081187)	Loamy sand	0.5	7.5	8.4
Rupert, ID 2008 (W15ID081188)	Loam	1.4	7.9	19.0
Wharton, TX 2008 (W05TX081189)	Silt loam	1.1	8.1	28.5

Maintenance chemicals or fertilizers were used at all trial sites during the study. Daily minimum, maximum, and average air temperatures during the trial periods were provided with the following exceptions: Jennings, FL, and Los Alamos, CA, were missing precipitation data and Los Alamos, CA, and Wharton, TX, were missing temperature data. Precipitation during May 2009 at the Jennings, FL, trial location was 5.38 inches above normal and March and April had precipitation more than 2 inches above normal. At the Gardner, ND, trial location, June, August, and September had precipitation more than 2 inches above normal. Precipitation at

Wharton, TX, was below normal for September (-2.13 inches), October (-3.01 inches), and December (-2.67 inches). Irrigation was utilized at all test locations but Gardner, ND, and Wharton, TX.

TABLE B.1.2. Study Use Pattern.

Location City, State; Year (Trial ID)	EP[1]	Application					Total Rate (lb ai/A)	Tank Mix/ Adjuvants[4]
		Method	Timing	Volume (gal/A)[2]	Rate (lb ai/A)	RTI[3] (days)		
Jennings, FL; 2009 (E13GA081181)	Difenoconazole 250EC	1. Foliar broadcast spray	BBCH 49	26.9	0.113	--	0.463	NIS at 0.125% v/v
		2. Foliar broadcast spray	BBCH 49	27.9	0.117	7		
		3. Foliar broadcast spray	BBCH 49	26.4	0.116	7		
		4. Foliar broadcast spray	BBCH 49	26.6	0.117	7		
Gardner, ND; 2008 (C12ND081182	Difenoconazole 250EC	1. Foliar broadcast spray	BBCH 45	21.4	0.124	--	0.472	NIS at 0.2% v/v
		2. Foliar broadcast spray	BBCH 46	20.3	0.117	7		
		3. Foliar broadcast spray	BBCH 46	19.1	0.116	8		
		4. Foliar broadcast spray	BBCH 49	20.0	0.115	6		
Madera, CA; 2008 (W30CA081184)	Difenoconazole 250EC	1. Foliar broadcast spray	BBCH 46	30.1	0.114	--	0.461	COC at 0.5% v/v
		2. Foliar broadcast spray	BBCH 47	30.2	0.115	7		
		3. Foliar broadcast spray	BBCH 47	31.0	0.118	7		
		4. Foliar broadcast spray	BBCH 48	30.1	0.115	7		
Madera, CA; 2008 (W29CA081185)	Difenoconazole 250EC	1. Foliar broadcast spray	3-inch long roots	30.3	0.116	--	0.462	NIS at 0.25% v/v
		2. Foliar broadcast spray	BBCH 75	30.0	0.115	7		
		3. Foliar broadcast spray	BBCH 75	30.3	0.116	7		
		4. Foliar broadcast spray	BBCH 77	30.5	0.116	7		
Fresno, CA; 2008 (W30CA081186)	Difenoconazole 250EC	1. Foliar broadcast spray	BBCH 46	30.1	0.125	--	0.471	COC at 0.5% v/v
		2. Foliar broadcast spray	BBCH 47	30.1	0.115	7		
		3. Foliar broadcast spray	BBCH 48	30.1	0.115	7		

TABLE B.1.2. Study Use Pattern.

Location City, State; Year (Trial ID)	EP[1]	Application					Total Rate (lb ai/A)	Tank Mix/ Adjuvants[4]
		Method	Timing	Volume (gal/A)[2]	Rate (lb ai/A)	RTI[3] (days)		
		4. Foliar broadcast spray	BBCH 49	30.2	0.115	7		
Los Alamos, CA; 2008 (W27CA081187)	Difenoconazole 250EC	1. Foliar broadcast spray	BBCH 43	43.7	0.114	--	0.462	COC at 0.5% v/v
		2. Foliar broadcast spray	BBCH 44	47.5	0.116	7		
		3. Foliar broadcast spray	BBCH 46	49.2	0.119	7		
		4. Foliar broadcast spray	BBCH 47	46.0	0.113	7		
Rupert, ID; 2008 (W15ID081188)	Difenoconazole 250EC	1. Foliar broadcast spray	BBCH 17	16.4	0.117	--	0.462	NIS at 0.425% v/v – no adjuvant added with first application
		2. Foliar broadcast spray	BBCH 17	15.7	0.116	6		
		3. Foliar broadcast spray	BBCH 19	16.2	0.116	8		
		4. Foliar broadcast spray	BBCH 41	15.6	0.113	8		
Wharton, TX; 2008 (W05TX081189)	Difenoconazole 250EC	1. Foliar broadcast spray	BBCH 13-15	20.4	0.118	--	0.463	COC at 0.25% v/v
		2. Foliar broadcast spray	BBCH 14-16	23.9	0.108	5		
		3. Foliar broadcast spray	BBCH 40-47	20.3	0.116	8		
		4. Foliar broadcast spray	BBCH 46-48	20.5	0.120	8		

[1]EP = End-use Product; Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole
[2] Gallons per acre.
[3] Retreatment Interval
[4] Adjuvant: NIS = non-ionic surfactant (Silicone, Induce or Preference) or COC = crop oil concentrate (HerbiMax, Dyne-Amic or Helena Crop Oil Concentrate)

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Carrot		
	Submitted	Requested	
		Canada	U.S.
1	--	NA	--
1A	--	NA	--
2	--	NA	--
3	1	NA	1
4	--	NA	--
5	1	NA	1
5A	--	NA	--
5B	--	NA	--

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Carrot		
	Submitted	Requested	
		Canada	U.S.
6	1	NA	1
7	--	NA	--
7A	--	NA	--
8	--	NA	--
9	--	NA	--
10	4	NA	4
11	1	NA	1
12	--	NA	--
13	--	NA	--
14	--	NA	--
15	--	NA	--
16	--	NA	--
17	--	NA	--
18	--	NA	--
19	--	NA	--
20	--	NA	--
21	--	NA	--
Total	8		8

B.2. Sample Handling and Preparation

Single control and duplicate treated samples of mature carrots were collected seven days after the last application. Additionally, carrots were also collected at DALAs of 0, 3, 10, and 14 days from the treated plot at Fresno, CA (W30CA081186) to obtain decline data. For the decline study, single samples of carrots were collected on the last day of application (0 DALA), 3 DALA, 10 DALA, and 14 DALA, with duplicate samples taken at 7 DALA. At all locations, each sample consisted of 12 large roots or 24 smaller roots for a minimum sample weight of approximately 5 lbs.

Harvested samples were sent frozen to the Syngenta facility (Greensboro, NC) for preparation for analysis. Samples were stored in freezers maintained at <-10 °C. Carrots were quartered and ground in a Hobart foodcutter. Dry ice was used as necessary to keep the samples frozen. All samples were shipped frozen via Federal Express overnight to Morse Laboratories (Sacramento, CA) and held frozen at <-20 ±5 °C until analysis. Samples were stored for 381 days (12.5 months) or less until extraction.

B.3. Analytical Methodology

Samples of carrots were analyzed for residues of difenoconazole with modified analytical method Syngenta REM 147.08 titled "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS". Additionally, carrot samples were analyzed for residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". Both methods have been reviewed previously by HED (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan). Brief descriptions of the methods were included in the submission.

Residues of difenoconazole in carrot samples were extracted by refluxing with methanol/concentrated ammonium hydroxide (80:20, v:v). Aliquots of the extracts were diluted with ultra-pure water, cleaned up using solid phase extraction, and analyzed using high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). The limit of quantitation (LOQ) was 0.01 ppm for difenoconazole for all matrices. The corresponding limit of detection (LOD) based on the smallest detectable standard was 0.000125 ppm.

Residues of metabolites T, TA, and TAA were extracted with methanol/water (80:20, v/v). Following the addition of Celite, the extracts were vacuum filtered, rinsed, and brought to volume with methanol/water (80:20, v:v). Individual aliquots of each extract were processed separately through solid phase extraction (SPE) cleanup and/or derivatization steps, which were specific for each analyte. Internal standard, specific for each analyte, was added to each aliquot prior to processing. Aliquots of the TAA extract were purified by solid phase extraction and then derivatized by HCl/butanol esterification. The TA aliquot underwent two derivatizations: an esterification using HCL/butanol and an acylation using heptafluoro butyric anhydride (HFBA). The T aliquot was directly derivatized with dansyl chloride to produce the dansyl derivative of 1,2,4-triazole and partitioned into ethyl acetate. All metabolite extracts were then evaporated to dryness, redissolved in acetonitrile/water (30:70, v/v), and analyzed using HPLC with mass spectrometric (MS/MS) detection. The LOQ (as respective parent equivalents) was 0.01 ppm for the triazole metabolites T, TA, and TAA. The LOD was 0.00003 ppm for T and TA and 0.00005 ppm for TAA in carrot.

The methods were validated in conjunction with the analysis of field trial samples. For concurrent recoveries, control samples of carrots were fortified with difenoconazole and the triazole metabolites (T, TA, and TAA) each at 0.01, 0.10, and 0.50 ppm. One control sample of carrots was also fortified with triazole alanine (TA) at 0.04 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations for samples of carrots are reported in Table C.2. The maximum storage duration from sampling to analysis was 381 days (12.5 months) for difenoconazole analysis and 356 days (11.7 months) for triazole metabolite analysis. All samples were analyzed within 0 to 6 days of extraction. Although no storage stability data were submitted with the subject study, available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on potato tubers are deemed adequate to support the storage intervals and conditions of carrot samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted carrot field trial data.

Concurrent method recovery data are shown in Table C.1. The LC/MS/MS methods used to analyze carrot samples for residues of difenoconazole and the triazole metabolites are adequate for data collection based on acceptable concurrent method recovery data. All concurrent method recoveries were within the acceptable range of 70-120%. Recoveries for difenoconazole were not corrected, since there were no residues detected in the associated control samples, while recoveries for metabolites were corrected when residues were detected in control samples. Fortification levels were adequate to bracket residues found in/on treated samples. Adequate sample calculations and chromatograms were provided.

Apparent residues of difenoconazole and triazole metabolites, 1,2,4-triazole (T) and triazole acetic acid (TAA), were below the LOQ (0.01 ppm) in/on all untreated samples of carrot. Apparent residues of triazole alanine (TA) were below the LOQ (0.01 ppm) in/on 8 of 13 samples of untreated carrot. Quantifiable residues of TA were observed in/on 5 of 13 samples of untreated carrot, at 0.012-0.025 ppm from four of the test locations. Quantifiable residues of TA in/on untreated samples were generally found at levels similar to or slightly less than residues found in/on treated samples from the same site.

Residue data from the carrot field trials are reported in Table C.3. A summary of the residue data is presented in Table C.4. Following four broadcast foliar applications of the EC formulation of difenoconazole plus adjuvant at a target total application rate of 0.46 lb ai/A, residues of difenoconazole ranged from <LOQ (0.01 ppm) to 0.203 ppm in/on carrots at a 7-day PHI. Residues of 1,2,4-triazole (T) were below the LOQ in/on all samples of carrots harvested 7 days following treatment. Residues of TA and TAA in/on carrot samples harvested at a 7-day PHI ranged 0.012-0.054 ppm and <0.01-0.013 ppm, respectively.

As shown in Figure 1, residue decline data show that residues of difenoconazole were relatively stable from the 0-day to 7-day sampling interval and then declined to <LOQ (0.01 ppm) by the 10-day sampling interval. Residues of T and TAA were at or near the LOQ (0.01 ppm) in/on all samples from the residue decline trial. Residues of TA in carrots fluctuated over the 14 day sampling period (ranging from 0.024 to 0.054 ppm) with no definite pattern of decline or accumulation.

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole.

Matrix	Analyte [1]	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%) [2]
Carrots (Root)	Difenoconazole	0.01	4	92, 91, 118, 109	103 ± 13.1
		0.1	4	86, 90, 98, 97	92.8 ± 5.9
		0.5	1	111	NA
	T	0.01	4	99, 77, 76, 90	85.5 ± 10.9
		0.1	4	99, 89, 97, 109	98.3 ± 8.4
		0.5	1	92	NA

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole.

Matrix	Analyte [1]	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%) [2]
	TA	0.01	3	89, 87, 100	92.0 ± 6.9
		0.04	1	85	NA
		0.1	3	90, 93	91.2 ± 2.3
		0.5	2	93, 94	93.3
	TAA	0.01	4	91, 93, 98, 106	96.7 ± 6.9
		0.1	3	97, 92, 102	96.8 ± 5.0
		0.5	1	98	NA

[1] T - 1,2,4-triazole; TA - triazole alanine; TAA - triazole acetic acid
[2] Standard deviation is only calculated for sample sizes ≥3.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Interval[1]	Interval of Demonstrated Storage Stability
		Difenoconazole	
Carrots (Roots)	At Syngenta facility: <-10 At Morse Laboratories: <-20 ± 5	53 - 381 days (1.7 – 12.5 months)	None provided with the subject submission; however, based on previously submitted storage stability data (DP#s 340379 and 356135), when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable at -20°C for up to two years in/on cotton seed, cotton oil, and cotton meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw.
		Triazole metabolites (T, TA, TAA)	
		53 - 356 days (1.7 - 11.7 months)	None provided with the subject study; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016).

[1] Actual storage duration from harvest to analysis. Samples were analyzed within 6 days of extraction.

TABLE C.3. Residue Data from Crop Field Trials with Difenoconazole.

Trial ID (City, State; Year)	Zone	Crop/ Variety	Commodity or Matrix	Total Rate (lb ai/A)	DALA[2]	Residues[1] (ppm)			
						Difeno-conazole	T	TA	TAA
Jennings, FL; 2009 (E13GA081181)	3	Carrot/ Apache	Root	0.463	7	<LOQ (0.0032)	<LOQ (0.0005)	0.016	<LOQ (0.0015)
						0.019	<LOQ (0.001)	0.012	<LOQ (0.0014)
Gardner, ND 2008 (C12ND081182	5	Carrot/ Tendersweet	Root	0.472	7	0.138	<LOQ (ND)	0.038	<LOQ (0.001)
						0.050	<LOQ (ND)	0.032	<LOQ (0.0006)
Madera, CA 2008 (W30CA081184)	10	Carrot/ Vitana F1	Root	0.461	7	0.010	<LOQ (ND)	0.040	0.012
						<LOQ (0.0098)	<LOQ (ND)	0.033	0.013
Madera, CA 2008 (W29CA081185)	10	Carrot/ Danvers Half Long 12G	Root	0.462	7	0.084	<LOQ (ND)	0.021	<LOQ (0.005)
						0.082	<LOQ (ND)	0.023	<LOQ (0.004)
Fresno, CA 2008 (W30CA081186)	10	Carrot/ Vitana	Root	0.471	0	0.017	<LOQ (ND)	0.034	<LOQ (0.009)
					3	0.017	<LOQ (ND)	0.024	<LOQ (0.006)
					7	0.015	<LOQ (ND)	0.054	<LOQ (0.009)
						0.021	<LOQ (ND)	0.054	0.011
					10	<LOQ (0.006)	<LOQ (ND)	0.041	0.014
					14	<LOQ (0.009)	<LOQ (ND)	0.047	0.013
Los Alamos, CA 2008 (W27CA081187)	10	Carrot/ Legend	Root	0.462	7	0.158	<LOQ (ND)	0.016	<LOQ (0.002)
						0.203	<LOQ (ND)	0.018	<LOQ (0.003)
Rupert, ID 2008 (W15ID081188)	11	Carrot/ Nantindo	Root	0.462	7	0.054	<LOQ (ND)	0.015	<LOQ (ND)
						0.059	<LOQ (ND)	0.016	<LOQ (ND)
Wharton, TX 2008 (W05TX081189)	6	Carrot/ Imperator 58	Root	0.463	7	0.037	<LOQ (0.002)	0.026	<LOQ (0.003)
						0.048	<LOQ (0.001)	0.020	<LOQ (0.003)

1 The validate LOQ for each analyte is 0.01 ppm. Reported values <LOQ (0.01 ppm) are presented in parentheses.
T - 1,2,4-triazole; TA - triazole alanine; TAA - triazole acetic acid. ND = Not detected.
2 DALA = Days after last application

TABLE C.4. Summary of Residue Data from Various Crop Field Trials with Difenoconazole.

Commodity	Analyte[1]	Total Applic. Rate (lb ai/A)	DALA[2]	Residue Levels (ppm)[3]						
				n	Min.	Max.	HAFT[4]	Median	Mean	Std. Dev.
Carrot (root)	Difeno-conazole	0.461 – 0.472	7	16	<0.01	0.203	0.181	0.049	0.062	0.059
	T	0.461 – 0.472	7	16	<0.01	<0.01	<0.01	ND	<0.01	NA
	TA	0.461 – 0.472	7	16	0.012	0.054	0.054	0.022	0.027	0.013
	TAA	0.461 – 0.472	7	16	<0.01	0.013	0.012	<0.01	<0.01	0.003

1 T - 1,2,4-triazole; TA - triazole alanine; TAA - triazole acetic acid
2 DALA = Days after last application
3 For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ (0.01 ppm) in Table C.3.
4 HAFT = Highest Average Field Trial.

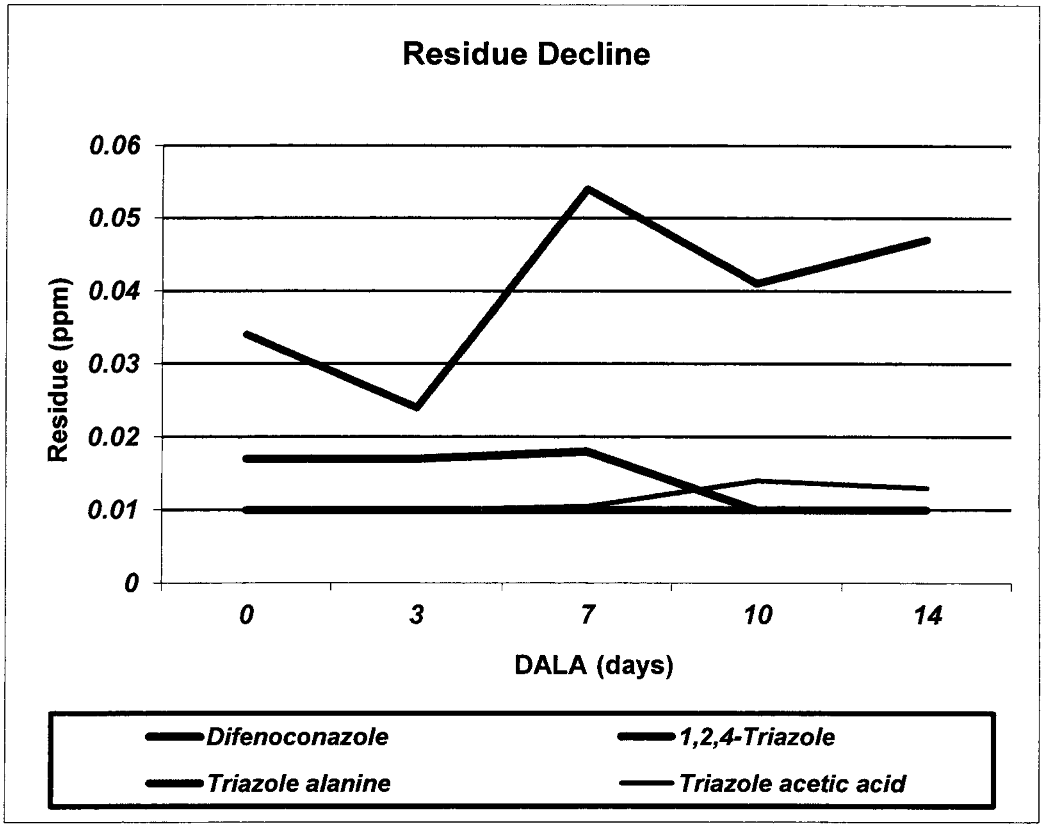


Figure 1. Residue decline in carrots from Trial W30CA081186 (Fresno, CA/2008).

D. CONCLUSION

The submitted field trial data reflect the use of four foliar applications of a 2.08 lb/gal emulsifiable concentrate formulation of difenoconazole on carrots at a target rate of 0.46 lb ai/A, with actual rates ranging from 0.461 lb ai/A to 0.472 lb ai/A. Spray volumes ranged from 15.6 to 49.2 GPA. Carrots were collected from each treated plot at 7 DALA at each trial. Additional samples were collected at 0, 3, 7, 10, and 14 DALA from trial W30CA081186 (Fresno, CA) to assess residue decline.

Acceptable methods were used for the determination of residues of difenoconazole and the triazole metabolites. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable, when stored under frozen conditions, for at least two years in/on potato tubers are deemed adequate to support the storage intervals and conditions of carrot samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted carrot field trial data.

Residue decline data for difenoconazole were generally stable from 0 to 7 DALA and declined to <LOQ by 10 DALA. Residues of metabolites T and TAA were generally at or below the LOQ. Residues of metabolite TA showed no discernable pattern of decline or accumulation over the 14-day sampling period.

No unusual weather phenomena were experienced during the conduct of this study. It does not appear that the agricultural practices used adversely impacted the results of the study.

E. REFERENCES

DP#:	172067 and 178394
Subject:	PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS# 9029, 9895.
From:	R. Lascola
To:	J. Stone/C. Giles-Parker
Dated:	10/26/92
MRIDs:	42090001-42090004, 42090032-42090059, and 42303901

DP#:	340379
Subject:	PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From:	W. Wassell/M. Sahafeyan
To:	D. Rosenblatt/S. Brothers
Dated:	8/9/07
MRIDs:	46950215-46950237

DP#	356135
Subject:	Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From:	B. Cropp-Kohlligian
To:	J. Bazuin/T. Kish
Dated:	9/17/09
MRIDs:	47413501 and 47413502

DP#	375159
Subject:	Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.
From:	B. Cropp-Kohlligian
To:	R. Kearns/T. Kish
Dated:	5/26/10
MRIDs:	47957001

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number(s): 9F7676
DP # 378829
PC Code: 128847

Template Version June 2005

Difenoconazole/CGA169374/PC Code 128847/Syngenta Crop Protection, Inc.
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3
Crop Field Trial - Chickpeas

Primary Evaluator: Bonnie Cropp-Kohlligian, Environmental Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Bonnie Cropp-Kohlligian

Approved by: Susan V. Hummel, Chemist/Senior Scientist Date: 2/23/2011
Risk Assessment Branch 4
Health Effects Division (7509P)
Susan V. Hummel

This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted (1/06/2011). The DER has been reviewed by HED and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

47929805. Willard, T.; Mayer, T. (2009) Difenoconazole - Magnitude of the Residues in or on Chickpeas: Final Report. Project Number: T004254-07, ML08-1489-SYN. Unpublished study prepared by Syngenta Crop Protection, Inc. 150 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection, Inc. has submitted field trial data for difenoconazole on chickpeas following four applications of an emulsifiable concentrate (EC) formulation containing 2.08 lb ai/gal (Difenoconazole 250 EC). Three chickpea field trials were conducted in the United States encompassing Zones 10 (CA; 1 trial) and 11 (OR; 2 trials) during the 2007 growing season.

Each field trial included one control plot and one treated plot in which the difenoconazole EC formulation was applied to chickpeas. Each plot was treated four times as a foliar broadcast application at a target rate of 0.115 lb ai/A, for a total seasonal nominal rate of 0.46 lb ai/A. Actual total application rates ranged from 0.4613-0.4627 lb ai/A in the chickpea plots. Re-treatment intervals were 14 days. Non-ionic surfactant was added to all spray mixtures. Single control and duplicate treated samples of chickpea seeds were harvested from each plot 14 days after the last application (DALA).

Samples of chickpea seed were analyzed for residues of difenoconazole using modified method Syngenta REM 147.08, "Residue Method for the Determination of Residues of Difenoconazole (CGA-169374) in Various Crops and Processed Crop Fractions" using liquid chromatography with tandem mass spectrometric detection (LC-MS/MS). Additionally, residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) were measured using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal Matrices". The limit of quantitation (LOQ) was 0.01 ppm for each analyte in all matrices. The methods were adequate for data collection based on concurrent method

recoveries.

The maximum storage duration from harvest to extraction for difenoconazole was 183 days (6.0 months) for chickpea seed and the maximum storage duration from harvest to extraction for the triazole metabolites was 157 days (5.2 months) for chickpea seed. All samples were analyzed within 4 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of chickpea samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted chickpea field trial data.

Following four broadcast treatment applications of difenoconazole at a total rate of 0.4613-0.4627 lb ai/A, difenoconazole residues were <0.01-0.032 ppm in/on chickpea seed (14 DALA). Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of chickpea seed; TA: 0.116-0.385 ppm in/on chickpea seed; and TAA: <0.01 ppm in/on all samples of chickpea seed.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document [DP#378829].

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: soil characterization, weather data, maintenance chemical applications, irrigation practices, and spray mix storage stability data were not collected under GLP. These deviations did not impact the validity of the study.

A. BACKGROUND INFORMATION

Difenoconazole is a broad-spectrum fungicide which belongs to the triazole (including the conazole) class of chemicals. It was developed under the code number CGA-169374.

The chemical structure and nomenclature of difenoconazole and the triazole metabolites are presented in Table A.1. The physicochemical properties of the technical grade of difenoconazole are presented in Table A.2.

TABLE A.1. Test Compound Nomenclature.

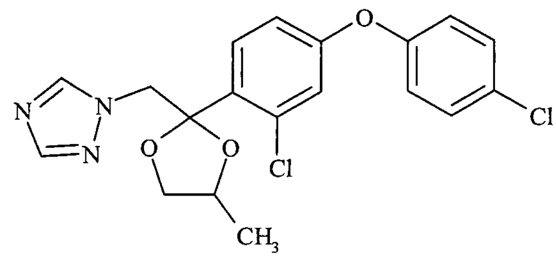
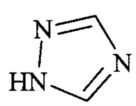
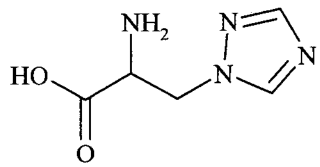
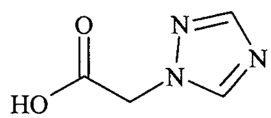
Compound			
Common name	Difenoconazole		
Company experimental name	CGA-169374		
IUPAC name	1-({2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl}methyl)-1H-1,2,4-triazole		
CAS name	1-[[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole		
CAS registry number	119446-68-3		
End-use product (EP)	Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole (Inspire®; EPA Reg. No. 100-1262)		
Compound			
Chemical name	Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

TABLE A.2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Melting point	78.6 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
pH	6-8 at 20 °C (saturated solution)	
Density	1.37 g/cm^3 at 20 °C	
Water solubility	3.3 ppm at 20 °C	

TABLE A.2. Physicochemical Properties of Difenoconazole.

Parameter	Value	Reference
Solvent solubility	g/100 mL at 25 °C: n-hexane: 0.5 1-octanol: 35 toluene: 77 acetone: 88 ethanol: 89	
Vapor pressure	2.5×10^{-10} mm Hg at 25 °C	
Dissociation constant, pK_a	pure grade (99.3% ± 0.3%) difenoconazole in water (with 4% methanol) at 20°C is 1.1	DP# 375159, 5/26/10, B. Cropp-Kohlligian
Octanol/water partition coefficient, $Log(K_{OW})$	4.2 at 25 °C	DP#s 172067 and 178394, 10/26/92, R. Lascola
UV/visible absorption spectrum	λ_{max} at about 200 and 238 nm (in methanol at 26 °C)	PMRA Proposed Regulatory Decision Document on Difenoconazole, 4/14/99 (PRDD99-01)

B. EXPERIMENTAL DESIGN

Three field trials were conducted on chickpeas in NAFTA Zones 10 (CA; 1 trial) and 11 (OR; 2 trials) during 2007 (Table B.1.1). The plots received four foliar broadcast applications, at 14 day retreatment intervals, of the 250EC formulation of difenoconazole. Each application was made at a rate of 0.1128-0.1179 lb ai/A for a total seasonal application rate of 0.4613-0.4627 lb ai/A. Applications were made using backpack sprayers and a spray volume of ~5 to 26 gal/A. Non-ionic surfactant was added to all spray mixtures.

B.1. Study Site Information

TABLE B.1.1. Trial Site Conditions.

Trial Identification: City, State; Year (Trial No.)	Soil characteristics			
	Type	%OM	pH	CEC meq/100 g
Madera, CA; 2007 (W29CA081201)	Loamy sand	0.5	8.2	6.9
Parkdale, OR; 2007 (W22OR081202)	Sandy loam	6.0	6.0	5.5
Hermiston, OR; 2007 (W21OR081203)	Loamy sand	0.8	5.8	12.4

Maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. The crop varieties grown are identified in Table C.3. The actual temperature and rainfall data were reported and no unusual weather conditions were noted during the field trials. Temperature and rainfall were within average historic values for the trial period.

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application Information					Tank Mix/ Adjuvants[5]
		Method; Timing (Crop growth stage)[2]	Volume (gal/A)[3]	Rate (lb ai/A)	RTI[4] (days)	Total Rate (lb ai/A)	
Madera, CA; 2007 (W29CA081201)	Difenoconazole 250 EC	1. Foliar broadcast; BBCH 69	25.29	0.1179	-	0.4627	NIS at 0.25% v/v
		2. Foliar broadcast; BBCH 71	25.82	0.1179	14		
		3. Foliar broadcast; BBCH 71	24.93	0.1141	14		
		4. Foliar broadcast; BBCH 77	24.66	0.1128	14		
Parkdale, OR; 2007 (W22OR081202)	Difenoconazole 250 EC	1. Foliar broadcast; first pods forming	5.05	0.1154	-	0.4619	NIS at 0.25% v/v
		2. Foliar broadcast; 77	5.23	0.1141	14		
		3. Foliar broadcast; pods reached final size	5.50	0.1172	14		
		4. Foliar broadcast; pods fully mature	5.10	0.1152	14		
Hermiston, OR; 2007 (W21OR081203)	Difenoconazole 250 EC	1. Foliar broadcast; 71	20.81	0.1162	-	0.4613	NIS at 0.125% v/v
		2. Foliar broadcast; 73	21.28	0.1159	14		
		3. Foliar broadcast; 75	21.35	0.1163	14		
		4. Foliar broadcast; 93	20.74	0.1129	14		

[1] EP = End-use Product; Difenoconazole 250 EC is an emulsifiable concentrate formulation containing 2.08 lb/gal difenoconazole.
[2] Difenoconazole was applied to chickpeas at 56, 42, 28, and 14 days prior to harvest for applications 1, 2, 3, and 4, respectively.
[3] Gallons per acre.
[4] Retreatment Interval.
[5] NIS = Non-ionic surfactant. Trials used Induce, X-77, or Silwet.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Chickpea		
	Submitted	Requested[1]	
		Canada	U.S.
1	--	NA	NR
1A	--	NA	NR
2	--	NA	NR
3	--	NA	NR
4	--	NA	NR
5	--	NA	NR
5A	--	NA	NR

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Regions	Chickpea		
	Submitted	Requested[1]	
		Canada	U.S.
5B	--	NA	NR
6	--	NA	NR
7	--	NA	NR
7A	--	NA	NR
8	--	NA	NR
9	--	NA	NR
10	1	NA	NR
11	2	NA	NR
12	--	NA	NR
13	--	NA	NR
14	--	NA	NR
15	--	NA	NR
16	--	NA	NR
17	--	NA	NR
18	--	NA	NR
19	--	NA	NR
20	--	NA	NR
21	--	NA	NR
Total	3		3

NR = Not reported.
[1] The Residue Chemistry Test Guidelines OPPTS 860.1500 reports in Table 1 that at least 3 trials are required for chickpeas. Distribution by region is not reported.

B.2. Sample Handling and Preparation

Single control and duplicate treated samples of mature dry chickpea seed were collected 14 days after the last application (DALA).

Samples were shipped frozen to the preparation facility, where they were stored at <-10 °C until sample preparation. Chickpeas were prepared for analysis by compositing and grinding with dry ice in a blender. The prepared samples were shipped frozen to Morse Laboratories (Sacramento, CA) and stored frozen at -20 ± 5 °C in temperature monitored freezers prior to analysis.

B.3. Analytical Methodology

Samples of chickpea seed were analyzed for residues of difenoconazole with modified analytical method Syngenta REM 147.08 titled "Residue Method for the Determination of Residues of Difenoconazole (CGA169374) in Various Crops and Processed Crop Fractions. Final Determination by LC-MS/MS". Additionally, chickpea seed samples were analyzed for residues of triazole metabolites, 1,2,4-triazole (T), triazole alanine (TA), and triazole acetic acid (TAA) using modified Morse Labs Analytical Method No. Meth-160/Revision#2, "Determination of 1,2,4- Triazole, Triazole Alanine and Triazole Acetic Acid Residues in Plant and Animal

Matrices". Both methods have been reviewed previously by HED (DP# 340379, 8/9/07, W. Wassell and M. Sahafeyan). Brief descriptions of the methods were included in the submission.

Residues of difenoconazole in chickpea samples were extracted by refluxing with methanol/concentrated ammonium hydroxide (80:20, v:v). Aliquots of the extracts were diluted with ultra-pure water, cleaned up using solid phase extraction, and analyzed using high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS). Residues of metabolites T, TA, and TAA were extracted with methanol/water (80:20, v/v). Following the addition of Celite, the extracts were vacuum filtered, rinsed, and brought to volume with methanol/water (80:20, v:v). Aliquots of the TAA extract were purified by solid phase extraction and then derivatized by HCl/butanol esterification. The TA aliquot underwent two derivatizations: an esterification using HCL/butanol and an acylation using heptafluoro butyric anhydride (HFBA). The T aliquot was directly derivatized with dansyl chloride to produce the dansyl derivative of 1,2,4-triazole and partitioned into ethyl acetate. All metabolite extracts were then evaporated to dryness, redissolved in acetonitrile/water (30:70, v/v), and analyzed using HPLC with mass spectrometric (MS/MS) detection.

The LOQ was 0.01 ppm for difenoconazole in chickpea seeds; the corresponding LOD was 0.000125 ppm. The LOQ (as respective parent equivalents) was 0.01 ppm for the triazole metabolites T, TA, and TAA. The LOD was 0.00003 ppm for T and TA and 0.00005 ppm for TAA in chickpea seeds.

The methods were validated in conjunction with the analysis of field trial samples. For concurrent recoveries of difenoconazole and metabolites T and TAA, control samples of chickpea seed were fortified at 0.01 and 0.1 ppm. For concurrent recoveries of the triazole metabolite TA, control samples of chickpea seed were fortified at 0.05 and 0.5 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are reported in Table C.2. Difenoconazole samples were stored at <-10 °C prior to extraction for analysis for 152-183 days (5.0-6.0 months) for chickpea seeds and triazole metabolite samples were stored for 126-157 days (4.1-5.2 months) for chickpea seeds. All samples were analyzed within 1 to 4 days of extraction. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of chickpea samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted chickpea field trial data.
Concurrent method recovery data are presented in Table C.1. The modified LC/MS-MS methods (Syngenta REM 147.08 and Morse Laboratories, Inc. Analytical Method No. 160 Revision 2) used for determining residues of difenoconazole and the triazole metabolites T, TA,

and TAA in/on chickpea (seed) were adequately validated in conjunction with the analysis of field trial samples. Concurrent recoveries were within the acceptable range of 70-120%.

Apparent residues of difenoconazole and metabolites T and TAA were <LOQ in/on all control samples of chickpeas. Residues of TA in/on control samples of chickpea were 0.024 to 0.033 ppm for seed. The petitioner attributed the occurrence of residues of TA in/on untreated samples to the widespread use of triazoles and the non-specific nature of the common moiety method of analysis. Adequate example chromatograms were provided.

Residue data from the chickpea field trials are reported in Table C.3. A summary of residue data for chickpea is presented in Table C.4.

Following four broadcast treatment applications of difenoconazole at a total rate of 0.4613-0.4627 lb ai/A, difenoconazole residues were <0.01-0.032 ppm in/on chickpea seed (14 DALA). Samples were also analyzed for T, TA, and TAA with the following residues: T: <0.01 ppm in/on all samples of chickpea seed; TA: 0.116-0.385 ppm in/on chickpea seed; and TAA: <0.01 ppm in/on all samples of chickpea seed.

TABLE C.1. Summary of Concurrent Recoveries of Difenoconazole and its Triazole Metabolites from Chickpea.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Seed	Difenoconazole	0.01	1	117	NA
		0.10	1	100	
	1,2,4-Triazole	0.01	1	93	
		0.10	1	99	
	Triazole Acetic Acid	0.01	1	97	
		0.10	1	102	
	Triazole Alanine	0.05	1	83	
		0.5	1	87	

TABLE C.2. Summary of Storage Conditions.

Matrix	Analyte	Storage Temperature (°C)	Actual Storage Duration[1]	Limit of Demonstrated Storage Stability
Chickpea, seed	Difenoconazole	<-10	152-183 days (5.0-6.0 months)	None provided with the subject submission; however, based on previously submitted storage stability data (DP#s 340379 and 356135), when stored under frozen conditions, residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for up to one year. In addition, residues are stable at -20°C for up to two years in/on cotton seed, cotton oil, and cotton meal; potato tuber; tomato, tomato paste, and tomato puree; sugar beet sugar, sugar beet dried pulp, and sugar beet molasses; and wheat forage, wheat grain, and wheat straw.
	Triazole metabolites (T, TA, TAA)		126-157 days (4.1-5.2 months)	None provided with the subject study; however, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016).

[1] Interval from harvest to extraction for analysis. Extracts were stored 1-4 days prior to analysis.

TABLE C.3. Residue Data from Chickpea Field Trials with Difenoconazole.

Trial ID (City, State; Year)	Zone	Crop/ Variety	EP[1]	Total Rate (lb ai/A)	DALA[2]	Residues (ppm)[3] Difenoconazole	T	TA	TAA
Madera, CA; 2007 (W29CA081201)	10	Chick pea/ UC-8537	Difenoconazole 250EC	0.4627	14	0.032 0.030	ND ND	0.385 0.381	<0.01 <0.01
Parkdale, OR; 2007 (W22OR081202)	11	Chickpea/ Sierra	Difenoconazole 250EC	0.4619	14	<0.01 <0.01	ND ND	0.166 0.195	<0.01 <0.01
Hermiston, OR; 2007 (W21OR081203)	11	Chickpea/ Sierra	Difenoconazole 250EC	0.4613	14	<0.01 <0.01	ND ND	0.122 0.116	ND ND

[1] End use product; 2.08 lb/gal EC formulation.
[2] DALA = Days after the last application.
[3] The validated LOQ was 0.01 ppm. TA = triazole alanine. TAA = triazole acetic acid. T = 1,2,4-triazole. ND = Not detected.

TABLE C.4. Summary of Residue Data from Crop Field Trials with Difenoconazole.

Commodity	Total Applic. Rate (lb ai/A)	DALA[1]	Residue Levels (ppm)[2]						
			n	Min.	Max.	HAFT[3]	Median (STMdR)	Mean (STMR)	Std. Dev.
Difenoconazole									
Chickpea, seed	0.4613-0.4627	14	6	<0.01	0.032	0.031	0.01	0.017	0.011
T									
Chickpea, seed	0.4613-0.4627	14	6	<0.01	<0.01	<0.01	<0.01	<0.01	NA
TA									
Chickpea, seed	0.4613-0.4627	14	6	0.116	0.385	0.383	0.181	0.228	0.124
TAA									
Chickpea, seed	0.4613-0.4627	14	6	<0.01	<0.01	<0.01	<0.01	<0.01	NA

[1] DALA = Days after the last application.
[2] TA = triazole alanine. TAA = triazole acetic acid. T = 1,2,4-triazole. Mean, median, HAFT, and standard deviations were calculated by the reviewer. The LOQ (0.01 ppm for all analytes) was used for calculations for any results reported as <LOQ in Table C.3.
[3] HAFT = Highest Average Field Trial.

D. CONCLUSION

The field trial data reflect the use of difenoconazole (EC formulation) as four foliar broadcast applications at a nominal rate of 0.115 lb ai/A per application for a total seasonal rate of 0.46 lb ai/A. The data reflect RTIs of 14 days and 14 days PHI for seed.

Acceptable methods were used for the determination of residues of difenoconazole and the triazole metabolites. No storage stability data were submitted with the subject study; however, available storage stability data indicating that residues of difenoconazole *per se* are stable in/on all raw agricultural commodities (RACs) for at least one year, when stored under frozen conditions, are deemed adequate to support the storage intervals and conditions of chickpea samples from the subject study. Furthermore, the U.S. Triazole Task Force (USTTF), whose members include Syngenta Crop Protection, Inc. among others, has submitted a multi-year storage stability study for the triazole metabolites in various crop matrices and processed commodities (MRID 47606601) which is currently under review in HED (DP# 363016) and these data are expected to satisfy storage stability data requirements for the submitted chickpea field trial data.

There was no unusual weather conditions reported that may have adversely impacted the results of the study. Additionally, it does not appear that the agricultural practices used adversely impacted the results of the study.

E. REFERENCES

DP#: 172067 and 178394
Subject: PP#2E4051. CGA-169374 (Difenoconazole, Dividend®) in Imported Wheat, Barley, and Rye Grain. First Food Use. CBTS# 9029, 9895.
From: R. Lascola
To: J. Stone/C. Giles-Parker
Dated: 10/26/92
MRIDs: 42090001-42090004, 42090032-42090059, and 42303901

DP#: 340379
Subject: PP#6F7115; Difenoconazole. Petition for Establishment of Tolerances on Fruiting Vegetables, Pome Fruit, Sugar Beets, Tuberous and Corm Vegetables, and Imported Papaya. Summary of Analytical Chemistry and Residue Data.
From: W. Wassell/M. Sahafeyan
To: D. Rosenblatt/S. Brothers
Dated: 8/9/07
MRIDs: 46950215-46950237

DP# 356135
Subject: Difenoconazole. Submission of Residue Analytical Methods Data in Response to DP#265858. Submission of Storage Stability Data in Response to DP#307059. Summary of Analytical Chemistry and Residue Data.
From: B. Cropp-Kohlligian
To: J. Bazuin/T. Kish
Dated: 9/17/09
MRIDs: 47413501 and 47413502

DP# 375159
Subject: Difenoconazole. Dissociation Constant in Water Data to Satisfy OPPTS 830.7370 Guideline Requirements.
From: B. Cropp-Kohlligian
To: R. Kearns/T. Kish
Dated: 5/26/10
MRIDs: 47957001

F. DOCUMENT TRACKING

RDI: Name1 (Date); Name2 (Date); Name3 (Date); etc.
Petition Number(s): 9F7676
DP # 378829
PC Code: 128847

Template Version June 2005.

R190280

Chemical Name: Difenoconazole

PC Code: 128847
HED File Code: 11000 Chemistry Reviews
Memo Date: 2/23/2011
File ID: 00000000
Accession #: 000-00-0137

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